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N.B.—*The Society does not hold itself in any way responsible for the statements made or the views put forward in the
various papers.*

United Services Section

President—Sir STANFORD CADE, K.B.E., C.B., F.R.C.S., M.R.C.P., Hon. F.F.R.

[*December* 3, 1953]

The Air Transport of Poliomyelitis Patients in Mechanical Respirators

By Group Captain R. L SOPER, F.F.A. R.C.S., R.A.F.

A MEMBER of the Armed Forces serving overseas, or a dependant, who becomes a victim of respiratory poliomyelitis, and requires to be nursed in a breathing machine, is a grave responsibility to his Medical Service. Such a case, requiring as it does a great deal of special attention, strains the facilities of the hospital abroad, which has usually only limited staff, to its utmost. Sisters and orderlies have to be devoted to his care only, relatives have to be accommodated; all the precautions of nursing an infectious case must be observed (at least in the early stages) and constant technical supervision of the apparatus is necessary. The patient himself usually wants to go home and clinical and administrative factors often render this desirable. Repatriation by air is the ideal, and indeed usually the only practicable, method. Such a facility is now part of the routine of the Royal Air Force's casualty evacuation service.

The idea of flying home a patient in an iron lung is not new. In July 1945 a case of respiratory poliomyelitis was successfully flown home to England from the R.A.F. Base in the Azores. He was carried in a cabinet type respirator, which, owing to electrical problems, had to be hand pumped throughout the journey.

In 1950 an officer's wife was flown home from Egypt. A Both cabinet respirator was used, but the pumping unit had been modified to suit the electrical system of the aircraft. This was a considerable advance on the Azores case, but a pumping team still accompanied the patient, in case of electrical failure, as well as the Medical Officer and the nursing sister.

The number of personnel employed, the size of the apparatus, and the all-important factor that at no time must the pump be allowed to stop operating, rendered this a complicated and costly procedure. The whole of a large transport aircraft was required to convey this one patient and his attendant staff. Normally, some twenty-eight stretcher cases are carried in such an aircraft.

A problem which gave rise to concern was that it was very difficult to secure the patient in such a way as to avoid movement caused by the forces of acceleration and deceleration of the aircraft. The only really fixed point in the patient-iron-lung system is the collar, and all forces tended to be transmitted to the patient's neck. It will be seen, therefore, that in the event of an imperfect landing, or any other sudden changes of the aircraft's movement, grave consequences might result to the patient. The only practical method of minimizing this, was for an attendant to stand at each side of the respirator, to hold the cabinet with one arm, and to insert the other through the armport, and to steady the patient by his shoulders. In the event of a major disturbance in the aircraft's speed or attitude, such precautions were likely to be of little avail.

The journey in the aircraft was not the only time when difficulty was experienced. The Both respirator consists of two units, the cabinet containing the patient, on its stand, and the pumping unit. The two are inter-connected by means of a flexible pipe. To get to the aircraft, a road journey is necessary. To get to the road, hospital corridors and lifts or stairs have to be negotiated. The whole paraphernalia has to be loaded and off-loaded, first on a road vehicle and later on to the aircraft. Should hand-pumping become necessary owing to electrical failure at this stage, things would be very awkward indeed.

It became obvious that some alternative method would have to be found.

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During the summer of 1950 various calls for air transport of iron-lung cases were received. Requests reached Air Ministry for an aircraft fitted with a respirator, to set off at a moment's notice, to bring home cases in the acute stage of the disease. On more than one occasion the aircraft turned back, whilst on its outward journey, because the patient had died after the signal had been sent. It became necessary to issue some instructions to avoid misunderstanding and wasted effort. Application for an air passage for a patient in a mechanical respirator, it was decided, should not be made until he had recovered from the acute stage of the disease. Further, the nearest R.A.F. Medical Specialist was to decide when a patient was ready to be transported. He should decide the best time for the journey, taking into account not only the patient's present condition, but the effect on the patient of the climatic conditions which would be encountered *en route*, and on arrival in the United Kingdom. In view of the highly technical nature of the undertaking, a team consisting of a Specialist Medical Officer, a sister trained to nurse in the air (with, if possible, a special knowledge of iron lung cases), and a technician, was to collect the patient.

To simplify the movement and to economize in space, it was decided to attempt to use a cuirass type of respirator for the next case which arose.

In November 1950 a request was made to the Air Ministry for the repatriation of a child from the R.A.F. Hospital in Ceylon. A cuirass respirator was borrowed from the Ministry of Health, and a team consisting of a flight sister, a technician and myself, left England with the apparatus. The outward journey took three and a half days, and the team, and our equipment were flown to Ceylon in an aircraft carrying a mixed cargo of passengers and freight. On arrival in Ceylon, five days were available before the aircraft returned, in which the patient could be weaned from the cabinet type respirator, in which he had been nursed up till then, and transferred to the cuirass respirator.

The child's general condition was worse than had been anticipated. In view of this, and because the apparatus had not been used by us for this purpose before, it was decided to give the child a test flight locally, before making a decision whether to undertake the journey home or not. The test was completely satisfactory, and a decision to bring the little patient home was taken. The return journey was made in three days with two night stops *en route*. As well as my patient, a load of casualties from Korea were carried. As the result of this journey, much valuable experience was gained, and the broad outlines of the present procedure were formulated.

Without wishing to exaggerate the difficulties, I would like to stress that this transport of patients in iron lungs is a complex procedure. A gravely ill patient, who may die at any moment, who is completely helpless and requires constant and expert nursing attention, is being conveyed in a machine, run by an electric motor, which must never be allowed, even for a moment, to stop. In the course of the journey he may be taken into, and out of, the aircraft on several occasions; there will be night stops in hospitals and journeys in ambulances. Apart from all other difficulties, these changes necessitate the constant alteration of the electrical supply. A flat battery, or an electrical plug which does not fit, would be enough to cause considerable difficulty. To give one example, the supply found at a hospital in Tripoli was of different voltage, and the plugs were of different standard, from any met anywhere else in my travels. Therefore, a considerable amount of organization is necessary, standardization is essential and special knowledge by each member of the team is *sine qua non*.

The Medical Officer in charge has to be prepared to meet various emergencies; should the patient become airsick and vomit, at the next stroke of the pump, this vomit may be drawn into his lungs. It is therefore highly desirable that, in the event of such a catastrophe, the Medical Officer should be able to use a bronchoscope. The technician, apart from being fully conversant with the workings of his apparatus, should be able to extemporize at a moment's notice, to cope with unexpected situations which he may find in the course of the journey. The nursing sister has the difficult job of gaining the confidence of the patient, who is nearly always apprehensive, and unhappy, when removed from the care of those to whom he has been accustomed.

Second only to the importance of his medical knowledge, is the Medical Officer's acquaintance with Air Force procedure. He must know whom to contact to get what he requires. He should be able to talk to aircrews, and other experts, in their own language. Whilst at all times remaining tactful, he should know when to insist, in the interest of the patient, and when he must defer to instructions, from branches other than his own.

Selected Royal Air Force Medical Officers are trained for these duties. After attending a short course they are sent on an ordinary casualty evacuation flight to accustom them to conditions of handling patients in the air.

During the training various points are stressed. First, that the patient must be in a suitable condition to undertake the journey. Gross cardiovascular insufficiency, or a severe degree of anæmia, is a contra-indication. Also the patient must be thoroughly accustomed to the portable respirator, and adequately ventilated by it. The apparatus is not as efficient as the cabinet type. The hæmoglobin should be at least 75% normal and, if low, the patient should be transfused before undertaking the journey. This can, of course, be done with advantage by the hospital staff, before the arrival of the team from England.

After first being fitted with the portable lung, a minimum of twenty-four hours continuous time spent in it is, in my experience, necessary before the return trip can be undertaken. Often, a great deal longer

may be required, before the patient is sufficiently accustomed to it to be flown home. When making use of the ordinary schedule flights, it may be necessary to stay over for the next one, if the patient is not ready on the day the aircraft is due to leave.

When a special flight has been made to collect a patient, off the ordinary evacuation route, Air Staff are apt to get worried if their aircraft and crew are unduly delayed. Appreciation of this point and an attempt to have all possible preliminaries, such as transfusions, &c., seen to before arrival of the team with the portable lung, will greatly assist them.

It must be remembered, however, that the final word on the transport of a patient is vested in the Medical Officer who comes to collect him. He must be given ample time and facilities to make his decision.

Perhaps this point is best illustrated by an example. A borderline case—one not actually in a lung but who might require one in the air—was sent on a long ambulance journey from the hospital to the airfield to meet the air ambulance. The Medical Officer had to make the difficult decision whether to take the patient, of whom he knew very little, and whom he had had no time to assess, or whether to return him to hospital, and make another trip to collect him later.

To date the only patient who could not be transported by the method now standard, was an advanced case of pregnancy. A cuirass type respirator is entirely unsuitable for such a patient.

The cuirass respirator is the only truly portable one at present generally available; and that is why apparatus of this type is used. It is quite possible that a portable cabinet respirator, which can be carried on a stretcher, with a compact pumping unit, will be made one day; and, if it is, it will have certain advantages over that at present employed.

The advent of a portable respirator of such a design, or the substitution of one of another make, would not materially alter the technique. The Monaghan respirator is now standard and is of American origin. Slight modifications have been made to the electrical system to suit special R.A.F. requirements.

Besides the respirator, medical equipment is taken by the Medical Officer consisting of instruments, drugs, oxygen for emergency use, and an electrical suction apparatus. The flight sister carries her standard kit of drugs and dressings, and the technician takes the tools of his trade.

[Rather than describe the procedure adopted in detail, the author showed a film made on this subject for instructional purposes.]

CONCLUSION

The time to bring the patient home is when he is convalescent, and only then if it is certain that the climatic conditions to which he is being returned are more favourable than those which he is leaving.

The final decision to take him home must remain with the Medical Officer who is going to be in charge of him throughout the journey.

Some Aspects of Rehabilitation in the Royal Air Force

By Squadron Leader C. B. WYNN-PARRY, M.B.E.

SOME of the results obtained in the residential rehabilitation centres in the Royal Air Force are presented in brief.

Of late the concept of rehabilitation has become wider and more fully accepted. It is more than ever essential in these days of economic difficulty to return patients to work as quickly as possible after injury or disease.

In the civilian field, increasing interest and research is developing in physical methods of treatment, and more rehabilitation centres are being established.

In the Royal Air Force cases are being sent earlier to the Rehabilitation Units, the Units are being used to their maximum capacity and the rehabilitation approach is spreading to all units.

These residential centres have three main advantages over the combination of sick leave and out-patient treatment. First, recovery is undoubtedly quicker. Not only does the patient regain physical health earlier, but also his confidence and ability to do his specific job. Secondly, the turnover of patients is accelerated and hospital waiting lists are cut down. Thirdly, they provide ideal conditions for studying difficult problems in diagnosis. Examples are the elucidation of the chronic low backache and the investigative treatment of suspected tears of the semilunar cartilages.

In 1951 over 3,000 patients were treated in the three Rehabilitation Units.

70% of these patients returned to full duty, 28% returned to modified duty and 2% were invalided from the Service.

Patients at Rehabilitation Units may be divided into short-term and long-term cases. Short-term patients are in the majority and almost all return to duty fully fit within a few weeks. Examples of this group are simple fractures and joint injuries, acute medical conditions such as post-pneumonia and bronchitis and post-operative surgical conditions.

Long-term cases include poliomyelitis, central nervous conditions, peripheral nerve injuries, multiple and compound fractures and cases of chronic backache. The majority of this group either return to modified duty in a lowered category or are invalided.

SHORT-TERM PATIENTS

The aim of treatment in the short-term patients is return to duty as quickly as possible. Advances are therefore to be expected in the development of techniques that will increase muscle power and accelerate the return of joint movement.

It is difficult to prove that rehabilitation of such short-term patients is economically sound, for although those who work in rehabilitation units recognize their value, it is almost impossible to show this statistically.

The ideal would be to present a series of figures comparing the rate of recovery with rehabilitation and the rate of recovery without, in a large range of orthopædic, medical and surgical conditions. For obvious reasons this is impossible. Moreover, it is a formidable task to compare different techniques of treatment in one injury, say fractures of the radius and ulna, when operative techniques involving plates, screws, nails, grafts, wire, and periods of plaster immobilization, vary so much.

Even more important is the scarcity of information on the actual result to be looked for in fractures and dislocations. None of the orthopædic textbooks gives more than a vague idea of the average range of joint movement to be expected after most fractures, or the time taken to reach that range.

We are at present comparing the results of treatment with various forms of physiotherapy, hydrotherapy, occupational therapy and remedial exercises in injuries of elbow, wrist, shoulder, knee and ankle.

This paper presents some of the preliminary results of this research, and also some of the results obtained in the commoner injuries seen at these centres.

Meniscectomies

Table I shows the results obtained in meniscectomies. The complications encountered in the 140 complicated cases appeared at the rehabilitation centre and not in hospital. They include effusions, gross muscle wasting, considerable laxity of lateral or cruciate ligaments, osteoarthritis and osteo-

TABLE I.—RESULTS OF MENISCECTOMIES

	No. of cases	Days in hospital	Days in rehabilitation centre
Uncomplicated	260	26	24
Complicated.. ..	140	25	48

chondritis dissecans. It will be seen that the average time from day of operation to day of return to duty in the simple cases of meniscectomy is 50 days. When complications are present, the time interval is doubled and many of these patients returned to duty in a lowered category or were invalided. The two main problems in treatment of meniscectomies are the prevention and treatment of knee effusions and the redevelopment of the quadriceps muscle. An investigation was carried out to determine the best method for accelerating the disappearance of a knee effusion (Millard and Wynn-Parry, 1953). There were 260 patients in the series in 95% of whom the effusion followed meniscectomy and in 5% was a simple non-operative traumatic effusion. All the patients were given six hours of remedial quadriceps exercises at the centre every day, and in addition five different treatments were investigated: (a) Support with a crepe bandage. (b) Constant current galvanism. (c) Application of a back splint and anodal galvanism. (d) Immobilization in a back splint. (e) Rest in bed with immobilization in a back splint (Table II).

TABLE II.—TREATMENT OF KNEE EFFUSIONS

Treatment	Days to disappearance of effusion	No. of cases
Class (exercises alone)	23·3	41
Class and crepe bandage	23·0	19
Class and galvanism	24·8	16
Class and galvanism and back splint	14·2	50
Class and back splint	10·3	115
Bed rest and back splint	9·4	19

It will be seen that complete and continuous immobilization of the knee in a back splint with intensive quadriceps exercises is the method of choice. It was concluded that the use of crepe bandages alone or of galvanism has no place in the treatment of knee effusions, and it is further suggested that rest in bed is not necessary to accelerate the disappearance of a knee effusion. It is now a routine measure to transfer patients from hospital to rehabilitation units after meniscectomy in a back splint, to prevent an effusion occurring during transit.

Millard (1951) has shown that daily electrical stimulation of the quadriceps is not of use in the redevelopment of the quadriceps muscle after meniscectomy unless there is gross muscular inhibition or wasting. Active exercises are always to be preferred, and it is hoped to present a comparison of various techniques for muscular redevelopment at a later date.

United Services Section

Table III presents a small series of cases of patellectomy. It will be seen that all patients who had their patellas removed for comminuted fracture recovered full joint range, and the average time from

TABLE III.—RESULTS OF PATELLECTOMY

Reason for operation	No. of cases	Days in hospital	Days at centre	Full range of movement
Fracture	12	46	51	All
Chondromalacia	15	48	75	12

day of operation to day of return to duty was 97 days. When the operation was performed for chondromalacia the time taken was 26 days longer, and as might be expected, not all regained full movement.

It was found that occupational therapy was particularly useful in the treatment of quadriceps lag and in regaining the last 30° of movement.

Table IV presents 53 cases of Putti-Platt repair for recurrent dislocation of the shoulder. The average time from day of operation to day of discharge with full range of movement (excluding external

TABLE IV.—RESULTS OF PUTTI-PLATT REPAIRS

No. of cases	Time immobilized (days)	Time at centre (days)	Range of abduction	Range of external rotation
53	40	33	Full	Full in 60%

rotation) and normal power was 73 days. It is interesting to observe that 60% obtained full external rotation, and no attempt was made to force this movement. It is our impression that active class exercises alone are needed to regain full movement and physiotherapy is needed only occasionally.

Table V presents the results obtained in a small series of upper limb fractures. Patients were discharged either when a full range of movement and normal power had been regained or when it

TABLE V.—RESULTS OF UPPER LIMB FRACTURES

Type of fracture	No. of cases	Time immobilized (weeks)	Time at centre (weeks)	Range of movement
Colles	21	8·5	3·8	Full
Greater tuberosity	19	9·0	6·0	Full abduction 50% Minimum range 120°
Mid-shaft:				
(a) Simple	35	9·7	4·5	Full abduction 83%
(b) Compound and comminuted	16	17·4	9·7	Full abduction 50%

was considered that no further progress would be made by full-time rehabilitation and the patient was fit for his specific job. It will be seen that the end-result of rehabilitation bears a direct relation to the severity of the injury and the time of immobilization.

Occupational therapy has been found helpful in building up the power of the shoulder muscles in severe injuries, for the resistance against which the patient works can be carefully graded and increased regularly.

In Tables VI and VII are presented the results of the two commonest fractures of the lower limb—Pott's fractures and simple fractures of the tibia and fibula. The average time from day of fracture to

TABLE VI.—RESULTS OF POTT'S FRACTURES

No. of cases	Type of fracture	Time (days) immobilized	Time (days) at centre	Range of movement
25	1°	48	43	Full
12	2°	67	67	Full
11	3°	66	74	Full in 4. 10° limitation in 7 (plantar flexion 4, inversion and eversion 3)

TABLE VII.—RESULTS OF SIMPLE FRACTURES

No. of cases	Time (days) immobilized	Time (days) at centre	Range of movement
24	78	56	Full 20 10° limitation 4 (plantar flexion, inversion and eversion)

day of discharge with full movement and power is four and a half months in simple fractures of the tibia and fibula. With Pott's fractures, the time for recovery is, as would be expected, dependent on the severity of the injury, and the time immobilized, though the subsequent range in 3rd degree

Pott's fractures was no more than 10° limited in any range. The time from day of fracture to day of discharge with full movements was 13 weeks with 1st degree Pott's and 19 weeks with 2nd and 3rd degree Pott's fractures. The important features in rehabilitation of leg fractures were found to be:

First, the necessity for careful education in walking at the earliest stage.

Secondly, the prompt control of post-plaster œdema, if necessary with special techniques such as faradism under pressure and careful bandaging, and

Thirdly, exercises with spring resistance for the calf muscles. If the patient walks with a flat-footed gait without sticks he does not use his calf muscles and hence special attention must be paid to these muscles in the physiotherapy department.

LONG-TERM PATIENTS

The main objective in these patients is first the early establishment of an accurate prognosis so that both Medical Officer and patient will know whether he will stay in the Service or have to be invalided, and secondly the treatment of the condition to produce maximum recovery possible.

Detailed study of the end-results of fractures, and a complete assessment of various types of treatment, as previously outlined, will go far towards establishing an early and accurate prognosis in severe and multiple fractures and joint injuries.

In the case of lower motor neurone lesions such as poliomyelitis and peripheral nerve injuries, modern methods of electrodiagnosis using strength duration curves and electromyography can give a remarkably accurate prognosis of recovery, as well as establishing a clear diagnosis in difficult cases.

Recent research in nerve injuries at Rehabilitation Units has shown that these electrical tests will give a forecast of recovery as long ahead as 8–12 weeks before the first clinical signs of recovery are seen. They will also give an accurate picture at an early stage of recovery as to whether function is likely to be good or poor and how long it will take (Wynn-Parry, 1953*a*, *b*).

In the event of the patient being invalided, it is the Medical Officer's responsibility to organize comprehensive resettlement. Good liaison exists between the Rehabilitation Unit, Disablement Resettlement Officer, Local Government Training Centre, local industry and Resettlement Branch of Air Ministry.

Finally, special appliances and gadgets are often necessary to enable the disabled patient to cope with the tasks of daily living, and it is the responsibility of the occupational therapy departments to devise and make such appliances for each individual patient.

In rehabilitation the co-ordination of effort of physiotherapist, occupational therapist and remedial gymnast is as vital to the successful treatment of the patient as the co-operation between the Orthopædic Surgeon, Medical and Surgical Specialist and the medical officers working in rehabilitation centres.

ACKNOWLEDGMENTS

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Section of Ophthalmology

President—HUMPHREY NEAME, F.R.C.S.

[*November* 12, 1953]

Report on a Case of Macular Degeneration of Familial Type, Tay's "Choroiditis", with Central Choroidal Atrophy as a Late Development.—HUMPHREY NEAME, F.R.C.S.

The patient, E. M., is a man aged 47, of sound general health. He was shown at the Section of Ophthalmology on December 9, 1938.

Vision was believed by him to have been defective from age 11 years, when he was tested by an optician. The diagnosis of macular degeneration was first made by Mr. Montague Hine in 1926 (age 20), when vision was R. 5/18, L. 5/18.

The patient knew of no relative with defective sight apart from a female cousin of his father. She was said to be highly myopic, and saw objects looked at but not the surroundings. (This might be explained by large temporal myopic crescents. H. N.) He had 3 brothers, all with good sight.

He was first examined by the writer in June 1930 when R.V. was 3/60 and L.V. 6/60 eccentrically. Each fundus oculi presented small aggregations of pigment spots in the centre of the macula. Very numerous colloid bodies (Tay's "choroiditis") surrounded this area and extended horizontally to a total extent of about 8 disc diameters. (Hamblin fundus drawings No. 1000/1927 and 1804/1931 show the approximate distribution of pigment and colloid bodies at this time.)

In January 1943, with vision reduced to 1/60 and 2/60, not improved by lenses, a strongly marked tigroid pattern was noted to extend over a circular area at the posterior pole of each fundus, with several densely black pigment clumps anterior to the outstanding choroidal vessels. This was presumed to be due to atrophy of pigment epithelium and choriocapillaris. A normal tigroid pattern was visible peripherally.

In spite of the very defective central vision he only gave up cycling early in 1947.

In December 1952, R.V. 1/60, L.V. 1/60, the larger choroidal vessels took on a tubular as opposed to the normal flat appearance owing to the atrophic state of the tissues anterior to them. This extreme degree of atrophy, showing white sclera between the large choroidal vessels, is strongly suggestive of another familial affection—central areolar sclerosis. Some of these exposed vessels show thickened walls and narrowed lumen.

This patient shows, combined in each eye, the signs of three entities that occur separately as familial degenerations—macular degeneration, Tay's "choroiditis", and central areolar choroidal atrophy.

Clinical Examination of the Vitreous Body

By K. HRUBY, M.D., Univ.-Augenklinik, Vienna

THERE are two ways of examining the vitreous clinically, by ophthalmoscopy and by slit lamp examination. The former is done in diffuse illumination, the latter mostly in the optical section, usually in the sagittal section. The diffuse illumination of the ophthalmoscope allows us to determine whether the vitreous is clear or opaque. It is possible to differentiate morphologically between dust-like, fibrous, discrete, membranous, strand-like opacities, &c., and sometimes to make a more complete diagnosis, as e.g. hæmorrhages, synchysis scintillans, foreign bodies, or air bubbles. It is difficult to localize the opacities exactly and to determine whether they are situated in the anterior face of the vitreous or in the framework, or in the posterior hyaloid membrane or in the subhyaloid space but changes in the vitreous not associated with visible opacities cannot be seen ophthalmoscopically at all. That is why the clinical diagnosis of vitreous changes was so limited prior to the introduction of slit-lamp microscopy.

Originally the slit lamp was designed for the examination of the anterior section of the eye only. The pioneers of the slit-lamp examination of the posterior section dealt with the problems by means of additional equipment. Nowadays slit-lamps are specially designed for the examination of the posterior section of the eye and the technique has been greatly simplified.

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Two main points are noteworthy in the optical adaptation of the slit lamp for the microscopy of the posterior section of the eye:

(1) The angle between the axes of observation and illumination (angle of incidence) has to be as small as possible but must not be 0° if the principle of lateral focal illumination is to be maintained.

(2) The fundus image has to be displaced optically so that it is located within the focal distance of the objectives of the microscope.

The first problem has been solved by reflecting mirrors (Koeppe), by Lindner's "angled microscope", by the reduction prism (Goldmann) and, finally, by the new combination of slit lamp and microscope that allows us to move the slit lamp from one side of the microscope to the other without any obstacle (Zeiss-Opton, A.I.M., &c.).

The second problem can be approached principally by strong plus and strong minus lenses. Evans (Brooklyn) and López Enríquez were not successful with convex lenses. The optical principle is identical with that of indirect ophthalmoscopy and, therefore, the observation gives an inverted image. Lately, new experiments have been performed to evaluate the advantages of this method. Strong minus lenses have been more successful. First of all, contact lenses have been applied (Koeppe, Goldmann, &c.). I recommended a preset lens of about − 55 dioptres myself. Comparing the two types of lenses there is a smaller visual field with a preset lens than with a contact lens. On the other hand, the preset lens offers several advantages: it can be handled very easily without annoying the patient. The examination can be repeated as often as necessary, and can be performed in children as well as in eyes that have been operated on or recently injured.

The accessibility of the fundus periphery is superior to that of the contact lens with which one can see the central parts of the fundus only. With the preset lens the image is less clear and less magnified than with a contact lens. But if the preset lens is well centred with the pupil, the least distortion of the image will result, and the loss of magnification can be compensated by a stronger resolving power of the microscope. The Zeiss-Opton slit lamp has been constructed so that it is possible to centre the preset lens automatically. I do not use a contact lens except in cases of optical disturbance such as irregular astigmatism, or in high myopia.

The examination of the vitreous has been improved by the mechanical and optical coupling of the microscope and the slit lamp. It is very difficult, if not impossible, to focus the microscope and the illumination separately on the delicate structures of the vitreous.

I developed the preset lens method in the slit lamp of Haag-Streit (Berne), so that I prefer this model for the examination of the vitreous. The manufacturing firm delivers the additional equipment necessary for the examination of the posterior section of the eye if desired. This consists of a preset lens mounted in a holder and of a fixation lamp, the light of which the patient is supposed to watch with the eye that is not being examined. The eye under examination is moved by means of this fixation lamp very satisfactorily. The utmost brightness of the slit illumination is essential for examination of the vitreous. For that reason, our model has been furnished with a transformer which allows us to increase the voltage from the normal 6 V up to 8 V. In addition, the flexibility of the holder of the preset lens permits us to put the preset lens as close in front of the patient's eye as possible. This is important; for the visual field increases with the decreasing distance of the preset lens from the eye. Finally, the preset lens can be moved in a frontal plane. This kind of decentration increases the accessibility of the periphery of the fundus because of the well-known prismatic effect of the high minus lens. The preset lens of the Zeiss-Opton slit lamp is fixed, but is centred to the microscope automatically. (I prefer this instrument mainly for examining the central parts of the fundus, particularly for macular lesions.) Unfortunately, the illumination of our Zeiss-Opton model is not quite bright enough to give the best diagnostic results in every case of delicate vitreous changes.

The examination of the vitreous with the slit lamp should always be preceded by that with the *loupe ophthalmoscope*. Then the experienced examiner knows what he may expect to see biomicroscopically. After this the anterior section of the eye including the *anterior part of the vitreous* is examined with the *slit lamp* in the ordinary way.

The posterior surface of the lens may show the physiological remnants of the hyaloid artery, the so-called Mittendorf's dot. It is located nasally to the posterior pole of the lens and occurs in young individuals in about 8% of all eyes according to Pellaton. Both the Mittendorf's dot and the white arc-line described by Vogt are not part of the lens capsule but of the anterior face of the vitreous and, therefore, this dot can be found sometimes following intracapsular cataract extraction.

The retrolental part of the vitreous shows little structural detail. It is identical with the primary vitreous and is separated from the secondary vitreous by the "membrana hyaloidea plicata". This membrane is said to be due to a condensation zone which continues the wall of Cloquet's canal, forward. It appears almost frontally in the eyes of adults because of the downward bowing of Cloquet's canal in postnatal life.

An *anterior detachment* of the vitreous, i.e. a visible detachment of the anterior hyaloid membrane from the posterior lens capsule, is a relatively rare observation. Senile eyes seem to have a tendency to anterior detachment and this may be an aid while extracting the cataract intracapsularly. Anterior vitreous detachment can be spontaneous or due to uveitis. In young patients a partial or

total anterior vitreous detachment can be found following severe trauma, e.g. perforating injuries of the eye, but they seldom occur spontaneously as in that following recurrent vitreous hæmorrhages.

The anterior part of the vitreous is relatively less accessible in myopic eyes than in hypermetropic ones for optical reasons. Here, we look for the *condition of the framework* of the vitreous and for *deposits* within the framework. The structure of the framework can vary within wide limits, and physiological and pathological findings are not to be distinguished easily. We are not able to attribute a certain pathological process to every type of structure seen or to make a final clinical diagnosis in every case. Often we have to limit ourselves to describing what we have seen. (Besides the normal structures thickening, rarefaction, irregularity, abnormal stratification, changes of motility can be found. Moderate destruction occurs in senility; marked destruction of the framework is seen in highly myopic eyes. Increased motility indicates liquefaction. An exact differentiation of the deposits, e.g. into inflammatory cells and blood cells, has been described by Koeppe, but it is not always possible to do this.)

The *posterior part of the vitreous* can be seen by means of a contact lens or a preset lens. Here, next to the fundus, only gross changes can be observed. Theoretically also pathological findings of the framework and pathological deposits can be distinguished. The normal structure of the posterior part of the vitreous appears *en bloc* only. This is also true with pathological changes. In a similar way, deposits in this part of the vitreous are not to be seen if they are too delicate. Large, isolated opacities appear grey-whitish in direct illumination, but almost black in reflected light. Thus they can be analysed optically. However, the diagnosis of a *posterior detachment of the vitreous* is much easier with the slit lamp than ophthalmoscopically. This superiority of the slit lamp also applies to the topographical localization of all associated changes of the framework, the posterior hyaloid membrane and the retrovitreal space.

The slit-lamp *examination of the posterior part of the vitreous* is done under more difficult conditions than that of the anterior section of the eye, and requires some training and experience; the optical section in this part of the vitreous is more or less disturbed by the bright diffuse light reflected from the fundus. The difficulty of observation is increased by the poor optical density of most of the structures in this region. Besides, the small angle of incidence decreases the resolving power in the optical section of successive structures sagittally. In spite of that the findings are surprisingly numerous.

(Here a series of illustrations were shown by the speaker.) Description alone could give the impression that some of the findings are the result of imagination rather than of true observation. Even A. Vogt, the outstanding expert of biomicroscopy, thought observations in the posterior part of the vitreous illusory rather than real. That is why the posterior section of the eye is not dealt with in Vogt's extensive textbook of biomicroscopy.

Without entering into the details of the special *technique of examination* I would like to emphasize the necessity of a well-dilated pupil, of bright slit illumination and of a dark-adapted examiner. The observation is predominantly done in direct as well as in reflected illumination. The lower power of the microscope is preferred. The optimal width of the slit varies from case to case and has to be changed during the examination. Within certain limits, the angle of incidence can be changed; it should be increased as much as possible but without destroying stereoscopic observation which is superior to monocular and therefore very desirable. A maximum of mydriasis, the closest possible position of the preset lens, hypermetropic refraction and reduction of the angle of incidence are favourable items in the slit-lamp microscopy of the posterior section of the eye.

Posterior detachment of the vitreous.—The most important and most frequent biomicroscopical findings in the posterior part of the vitreous are due to the *posterior detachment of the vitreous*. This condition is defined by a separation of the posterior hyaloid membrane from the optic disc and the retina in an extensive area behind the ora serrata associated with a more or less marked retraction from the retina towards the vitreous base. Thus the vitreous cavity is divided into two parts: one that is filled with the retracted vitreous and the other, the retrovitreal space, that contains nothing but the retrovitreal fluid.

Posterior detachment of the vitreous is a relatively common condition. In myopia the onset of a posterior detachment of the vitreous can be predicted by the degree of the myopia and the age of the patient according to Rieger. Other favourable conditions are senility, inflammatory reactions of the anterior and posterior uvea, contusions, perforating injuries and intra-ocular operations, cases of retinal detachment with tears, hæmorrhages of the vitreous cavity and cases of retinitis proliferans or tapeto-retinal degenerations.

The diagnosis is often possible by means of the *loupe ophthalmoscope* with which *opacities of the posterior hyaloid* membrane can be revealed. These multiform, discrete opacities are the cardinal ophthalmoscopic symptom of the posterior detachment of the vitreous. According to Rieger these opacities are made up of preformed glial tissue originating from the surface of the optic disc or from other parts of the fundus, e.g. areas of inactive choroiditis, and remaining in connexion with the posterior hyaloid membrane. The most impressive of these discrete opacities are the prepapillary ring-shaped, often fenestrated, opacities. In addition, there are numerous kinds of different opacities in the prepapillary area, but not infrequently also somewhere else in the vitreous cavity.

Biomicroscopical diagnosis of the posterior detachment of the vitreous.—This is based upon the visibility of the detached posterior hyaloid membrane in focal illumination. This posterior hyaloid membrane separates the framework of the retracted vitreous that shows a certain degree of flare from the optically empty retrovitreal space. The optical density of the posterior hyaloid membrane varies individually and locally and the membrane cannot be demonstrated in every case and in full extent with identical distinctness. But, with discrete opacities already found ophthalmoscopically a posterior detachment of the vitreous can be taken for granted with certainty. The discrete opacities help us to find the site of the posterior hyaloid membrane. We look for them in the central region first by investigating the vitreous cavity carefully in an antero-posterior direction or vice versa with the coupled slit-lamp system. Not infrequently the posterior hyaloid membrane can be demonstrated first in a peripheral area. With the posterior hyaloid membrane recognized in a certain area its course and the shape of the vitreous detachment can usually be found easily.

Complete and partial detachment of the vitreous.—In eyes with *complete detachment* the vitreous detachment is present everywhere in the fundus behind the ora serrata. Complete detachment of the vitreous is supposed to be the most frequent result of every partial detachment of the vitreous that has started somewhere behind the ora serrata. The two most important types of complete posterior detachment of the vitreous are the *simple* and the *collapsed*. The *simple posterior detachment* is characterized by the following topographical points: The posterior hyaloid membrane is about equally retracted from the optic disc as well as from the other parts of the fundus, and at first maintains its spherical shape. However, with increasing retraction the posterior hyaloid membrane appears "tautly stretched" within a short distance behind the lens. This simple form of complete posterior vitreous detachment does not occur typically in myopic and old individuals. The second main type, the *collapsed* detachment, shows a marked collapse of the vitreous due to advanced destruction and liquefaction of the framework. The sagittal section reveals the posterior hyaloid membrane extending frontally and relatively close behind the lens in the upper part, but sagittally in the central region, and arching downwards close to the fundus, and extending again forward towards the lower ora serrata. The collapsed vitreous is apparently suspended in the retrovitreal fluid because of the similar specific gravity of both materials. The "*funnel-shaped*" vitreous detachment that has been considered fairly common by former authors is relatively rare. It represents an almost complete posterior detachment of the vitreous associated with a circumscribed connexion of the posterior hyaloid membrane with the optic disc or another area of the fundus. This connexion being unusually tight prevents detachment of the vitreous in this particular area. Finally, there are *irregular types* of posterior detachment of the vitreous that can be observed following cataract extraction or perforating injuries with loss of vitreous.

Partial detachment of the vitreous is more infrequent and is usually the early stage of progressive, complete detachment. According to its site we can differentiate between upper, posterior, lateral and lower detachment. Finally, there are the irregular types.

Following the diagnosis and the morphological differentiation of the vitreous detachment we may look for more details. The multiform discrete opacities can be localized in the posterior hyaloid membrane without difficulty. This membrane often shows up round *defects*, particularly within discrete opacities. Again, there is the prepapillary fenestrated vitreous ring. Hernia-like invaginations of vitreous framework backward through these defects can be observed occasionally. Isolated cord-like connexions between the detached posterior hyaloid membrane and the optic disc or pathologically altered areas of the fundus can be found sometimes; they are not necessarily identical with a persistent hyaloid artery. In rare cases a true persistent hyaloid artery is seen extending from the lens to the detached posterior hyaloid membrane, or through a defect in this membrane to the optic disc. Very seldom, the posterior hyaloid membrane can be found detached from the vitreous itself. With the posterior hyaloid membrane being recognized and topographically determined, ophthalmoscopically and biomicroscopically visible opacities and changes of the vitreous can be localized more accurately. Thus the differentiation between changes and deposits of the framework, discrete opacities in the back membrane and changes in the subhyaloid space is possible. "*Vitreous cysts*" as seen by many authors proved to be spherical opacities of the posterior hyaloid membrane (Rieger). *Hæmorrhages* in the vitreous cavity can be limited to the subhyaloid space, or they can be seen invading the framework of the vitreous through breaks of the posterior hyaloid membrane. Similar findings are found with *intra-ocular foreign bodies* that often do not penetrate the framework of the vitreous, but move and stay between the retina and the detaching posterior hyaloid membrane. In cases of *retinitis proliferans*, the slit lamp reveals that the connective tissue and the blood vessels proliferate within the subhyaloid space and along the posterior hyaloid membrane which acts as an impenetrable barrier.

The results of examinations of the vitreous in eyes with *spontaneous retinal detachment* contributed to the argument about the origin of the primary retinal defects. Numerous examinations of mine revealed the fact that the primary tears are caused by the shock-like pulling action of the vitreous as postulated by the theory of Leber, Gonin and Lindner. In most of these cases the connexion of the detached vitreous with the operculum can be proved clinically with the slit lamp. This connexion

of the posterior hyaloid membrane with the operculum of the retinal tear is not separated by the operation and, therefore, should be kept in mind during the operation. On the other hand, no similar connexion is present in Vogt's cases of purely *degenerative holes*. However, *"borderline"* *cases* may occur. These are found in the lower half of the fundus, appear to be degenerative holes and are located exactly at the site where the detached vitreous is adherent to the retina. In such cases both retinal degeneration and the pulling action of the vitreous collaborate in producing the retinal defect. For these reasons it is impossible to label clearly every retinal defect as coming into a special category.

My own examinations of about 200 eyes with retinal defects showed a ratio of three tears to two holes. Both kinds of defect differ in *topography* according to the causative mechanism. The pulling action of the vitreous is more effective in the upper half of the fundus because of gravity. Degenerated retina is torn more easily than normal retina. Cystoid retinal degeneration and retinal atrophy are likely to occur in areas of the poorest blood supply, namely in the temporal periphery and in the macular region. Both components, the retinal degeneration and the pulling action of the vitreous, are additive in the upper temporal quadrant which shows the most frequent incidence of retinal tears. The upper nasal and the lower temporal quadrant follow. The lower nasal quadrant rarely shows retinal tears. Degenerative holes of the retina are mostly found in the macular region, and in the temporal periphery, the usual sites of retinal degeneration. The lower temporal quadrant is the most frequent site of degenerative holes whereas the upper temporal quadrant is more prone to show tears because the pulling action of the vitreous usually becomes effective before the retinal degeneration has led to hole formation.

Relative frequency of retinal detachments.—There is no obvious explanation of the statistically proved fact that retinal detachment and retinal defects occur in the right eye more often than in the left.

My research work was also directed towards ascertaining whether the defect formation in an individual is specific or not, i.e. the probability of the incidence of the same kind of defect in recurrent or bilateral detachments. In 20 matching cases different defects occurred in only 4 instances. This speaks for an apparently limited tendency to constancy in defect formation. One case of familial retinal detachment is noteworthy in that hole formation occurred in one eye, tear formation in the other eye in the case of the mother, whilst there was bilateral hole formation in the case of the daughter.

Another interesting point is the distribution of retinal defects in myopic and in non-myopic patients with retinal detachment. Retinal tears are present in 60% of both groups. In myopic patients retinal holes occurred with equal frequency in the macular region and in the periphery. In non-myopic patients, however, primary holes of the macular region are rather rare.

The average age of the patients with retinal tears is slightly higher than that of the patients with holes, but the difference is not significant. The average age of the myopic patients is lower in both groups than that of non-myopic patients. This proves once more the fact that the myopic eye is an early ageing eye from the biological point of view.

The form of vitreous detachment which plays the most active role in the pathogenesis of retinal detachment is probably that of *complete posterior vitreous detachment of the collapsed type*. The simple type is of minor importance, the upper vitreous detachment is a definite rarity.

Prognosis.—Retinal tears should be considered of less favourable prognosis than retinal holes because of the continuing pulling action of the vitreous. This is only true, however, after the unfavourable cases of macular holes in eyes with high myopia and central choroidal atrophy have been eliminated. We could then achieve a successful surgical result in 77% of retinal detachments with hole formation in comparison with 67% of those with tears. The difference is small and the prognosis depends on other factors as well.

Oral disinsertions.—Further, our investigations of the vitreous contributed to the evaluation of *oral disinsertions*. Biomicroscopically, we are able to differentiate two types. In a proportion of the cases, the detached vitreous is disinserted from the ora serrata together with the retina, both tissues firmly adherent to each other along the edge. A retinal cyst can be found adjacent to the edge of the defect, but this is—as far as I know—a rare condition. The second group does not show any connexion between the vitreous and the retina, and the posterior hyaloid membrane is seen extending towards the periphery, probably being attached at the peripheral edge of the retinal defect, very similar to true tears. Accordingly, we could call the former ones oral disinsertions, in a closer sense the latter ones oral tears. Both kinds of oral defects can be differentiated from each other also ophthalmoscopically. The disinsertion is not too extensive, and is occasionally divided into several sections by bridging retina. The posterior edge of the defect is grey-white and thickened and does not show any tendency to coil up. The oral tear may be a giant tear, its posterior edge is thin and often it is coiled up. In very big tears the peripheral retina can turn over and the outer retinal surface can be seen as a greyish membrane. The oral tears are caused by a similar mechanism to retinal tears with operculum, but the origin of disinsertions is not clear. Probably, the main factor is post-traumatic or spontaneous retinal degeneration. We cannot deny the detached vitreous has a share in causing the defect, since similar cases may be observed following perforating injuries

associated with shrinkage of the vitreous. Disinsertions occur mostly in non-myopic eyes, oral tears are more frequent in high myopia. Both types of oral defect find their topographical parallel in the retinal tears as well as in the retinal holes. Oral disinsertions offer a fair prognosis, oral tears are less favourable.

Biomicroscopically, *adhesions of the detached vitreous to retinal vessels* can be observed not infrequently, a condition already proved histologically by Rieger. Such adhesions may be considered physiological vitreous-retinal synechiæ capable of becoming focal points of vitreous shock and thus of precipitating a retinal tear. Indeed, retinal vessels are often seen crossing over retinal tears and it is well known that the tear formation sometimes coincides with extensive hæmorrhages into the vitreous cavity due to the laceration of blood vessels.

The condition of the vitreous in cases of *real traumatic detachment of the retina* differs biomicroscopically from that in spontaneous retinal detachment. Real traumatic detachments occur in normal eyes following direct or severe indirect trauma. We could not find any connexion between the detached vitreous and the retinal defect that is likely to be caused by traumatic degeneration of the retina.

The clinical importance of vitreous examination.—The onset of a posterior vitreous detachment in myopic, senile and other eyes is often associated with photopsia, entoptic perception of discrete opacities or other low-grade visual disturbances that sometimes alarm the patient. Occasionally the sudden and striking onset of subjective symptoms justifies Benziger's term "acute vitreous detachment". Even slight hæmorrhages of the retina and of the vitreous have been reported. Biomicroscopy may prove the presence of a vitreous detachment causing the subjective symptoms, even in cases that are negative, or doubtful or obscure on ophthalmoscopical examination. Other patients who have full visual acuity complain of a delicate, moving veil disturbing their sight. They usually show a posterior vitreous detachment with little retraction not revealed by the ophthalmoscope because of the optical delicacy of the posterior hyaloid membrane.

The onset of a posterior vitreous detachment is almost always of no harm to the eye and is seldom followed by a retinal tear and detachment. Apparently different factors have to be present in order to elicit a retinal tear. Collapsed and irregular types of vitreous detachment associated with isolated synechiæ of the vitreous with the retina in degenerated areas seem to play a conditioning role. Posterior vitreous detachment as well as discrete opacities or morphological changes of the framework are not accessible to therapeutic measures. Usually, the disturbing symptoms improve gradually with increasing retraction of the posterior hyaloid membrane from the retina, with advancing collapse of the vitreous associated with the downward displacement of the discrete opacities into the lower periphery of the vitreous cavity, and also with the patient's becoming used to the condition. This apparent improvement is usually attributed to any and all kinds of treatment.

Sometimes the diagnosis of a posterior vitreous detachment reveals another pathological condition, e.g. an anterior choroiditis or a latent retinal tear. Discrete opacities located close in front of the retina may cause a reddish shadow that has been confused with a retinal hæmorrhage and thus has caused errors in therapy and in prognosis. Occasionally, the defects in a fairly dense posterior hyaloid membrane resemble retinal defects because of the similar reddish appearance. Discrete opacities or proliferations of connective tissue along the posterior hyaloid membrane, as seen following intra-ocular hæmorrhages, may possibly be confused with intra-ocular foreign bodies ophthalmoscopically. Densification of the detached vitreous or of the hyaloid membrane is capable of causing a diffuse haziness of the fundus not to be determined ophthalmoscopically. Diffuse haziness of the fundus in a circumscribed area associated with the subjective symptoms may be supposed to be an early detachment. This is especially true with extensive vascularized membranes in cases of retinitis proliferans which resemble a retinal detachment or an intra-ocular tumour. Biomicroscopical examination can usually clarify the diagnosis.

Intra- and retro-vitreal hæmorrhages can be differentiated. In the latter prognosis is more favourable than in those that have invaded the framework of the vitreous. Intra-ocular foreign bodies and parasites can be localized in their relationship to the detached vitreous biomicroscopically and, thus, the most suitable operation can be chosen.

Cases of *retinal detachment* always call for an exact investigation of the vitreous. A collapsed or simple detached vitreous does not prevent a reattachment of the retina. However, in cases of *tightly stretched posterior hyaloid membrane*, as seen in already operated cases of retinal detachment, or in aphakia, or following perforating injuries or intra-ocular hæmorrhages, diathermy alone cannot be expected to cure the retinal detachment. In such cases a scleral resection or a combination of diathermy and scleral resection has to be performed. But even the latter procedure is unsuccessful if the detached retina is adherent to the tautly stretched hyaloid membrane in an extensive area.

An unintentional perforation of the retina by diathermy would be the more dangerous the more vitreous is still present, since the detached vitreous responds to the leaking of the vitreous cavity by retracting and thus preventing the reattachment of the retina. That is also the reason why we do not like to perforate at the site of the tear, but do so close to it. Hæmorrhages of the vitreous cavity following surgical procedures for retinal detachment do not offer a favourable prognosis except

in those cases with little vitreous present. For these, hæmorrhages cause further shrinkage of the framework. The width of the scleral strip to be excised is determined by the volume of fluid in the subretinal and subhyaloid space, the depth of which can be estimated biomicroscopically rather than ophthalmoscopically.

The site of the detached posterior hyaloid membrane and its course may be capable of indicating the location of a retinal defect. Finally, the knowledge of a connexion between the vitreous and the operculum of the tear forces us to consider using a very strong diathermy current in the area of the base of the operculum since we have to meet with the continuing pulling action of the vitreous. The posterior edge of the retinal tear can be treated with less intensive diathermy.

The absence of a posterior vitreous detachment in cases of retinal detachment probably argues against a primary detachment and should make us think of an intra-ocular tumour.

Other differentiating problems in cases of retinal detachment are easily solved by biomicroscopical examination, but this does not belong to this paper.

Conclusion.—Biomicroscopical examination of the vitreous is of great clinical importance. My aim in this address has been to give practical points rather than theoretical knowledge and I hope I have demonstrated that biomicroscopy of the vitreous is no mere ophthalmological hobby.

The President said that Dr. Hruby had spoken of a loupe ophthalmoscope. He presumed he meant the ophthalmoscope with a + 10 D or other lens.

Sir Stewart Duke-Elder remarked that there was only one thing he objected to in Dr. Hruby's paper, namely, that he had given an impersonal name to what in this country they had always been accustomed to call the Hruby lens. It was more interesting and suitable to retain the memories of this lecture by using the personal name. Dr. Hruby's remarks about holes in the retina were interesting. It had always worried him that when they closed a retinal hole vitreous adhesions at this site might be a potential cause of another hole. He wondered whether that worried Dr. Hruby and, if so, whether there was anything that could be done about it.

Mr. R. Affleck Greeves said that he had learned a great deal from Dr. Hruby's paper. For a number of years he had thought that often what were called vitreous opacities were not in the vitreous itself but in a space behind it. Could Dr. Hruby throw any light on a certain condition familiar to most ophthalmic surgeons? This concerns middle-aged and elderly patients who complain of seeing transient flashes of light, the flashes persisting for variable periods, sometimes only for a few days, in other cases for weeks or even months. These flashes are accompanied by the development of opacities in the vitreous. His experience was that in these cases the vitreous opacities became gradually less noticed by the patient; this, of course, might be attributed partly to the patient having been reassured that the condition was not a serious one, and partly to the patient's having got used to the floaters.

On retinitis proliferans Dr. Hruby's remarks had been very enlightening, because, in his opinion, he had explained why the characteristic bands of fibrous tissue become attached to the periphery by a process of creeping along the surface of the hyaloid membrane, and so forming a peripheral attachment. Had Dr. Hruby ever noticed in the course of his investigations minute linear opacities in the normal vitreous? He himself had occasionally seen such strands in the course of routine microscopical examinations, and he had thought it possible that they might be the remnants of hyaloid vessels, and might constitute the so-called "muscæ volitantes".

Mr. H. B. Stallard asked whether Dr. Hruby had made any observations in cases in which sterile air had been injected into the vitreous at the end of the retinal separation operation.

Mr. C. Dee Shapland asked whether Dr. Hruby had had any experience of dividing vitreous bands such as are usually seen after perforating injuries and intra-ocular foreign bodies and which often produce a traction retinal detachment. The speaker had always regarded this as a hopeless procedure. He was also interested to note that Dr. Hruby had also found a slightly greater incidence of retinal detachment in the right as compared with the left eye, a preponderance which had constantly occurred in Mr. Shapland's many series of detachment cases.

Mr. Arthur Lister, speaking on the question of the development of opacities preceded by flashes of light, said that he recalled one patient who experienced the flashing of light one evening and the next morning there was a large vitreous floater in the right eye. The same thing occurred subsequently in the left eye. He concluded that the flashes were due to adherent vitreous becoming detached from the retina, causing a flash of light at that particular point. If the vitreous pulled the retina off with it, causing a tear, a retinal detachment would develop. There was one possible idea that had occurred to him inspired by Dr. Hruby's lecture and that was that in cases when vitreous adhesion was preventing retinal replacement it might be possible to inject air behind the "solid" part of the vitreous, break the adhesion, and thus allow the retina to go back.

Mr. A. Hollingsworth had noted that the lightning flashes were always on the temporal side. He had never come across anyone who had seen them on the nasal side.

Mr. G. W. Black wondered whether Dr. Hruby could give them some estimate of the value of scleral resection. A colleague had recently said that he would need to do 75 cases before he got a success! A somewhat pessimistic outlook. As he understood the lecturer there might be, in some cases, a need for one or two sclerectomies to adapt the size of the sclera to the shrunken vitreous. Did this process of retraction of the vitreous continue, and if so was there likely to be a need for further sclerectomies in the future?

Air Commodore J. C. Neely spoke of the extraction of foreign bodies. In view of the damage occasioned to the vitreous would it be advisable to apply diathermy in a ring around the foreign body or not?

Mr. J. Gourlay said that, with reference to Mr. Black's statement, the exact point was that on the basis of 25% of successes, a man might have to do 75 scleral resections before obtaining a success. Was there any place for vitreous replacement in intra-ocular hæmorrhage which had not reabsorbed after a year or eighteen months?

Mr. J. D. J. Freeman asked the lecturer's opinion on solidity of the vitreous such as was found frequently in high myopes. One got the impression in some of these cases that the vitreous was disorganized. Would he say that the vitreous had been detached with a large amount of sub-hyaloid fluid?

Mr. R. J. Buxton said that he believed he was the first British ophthalmologist to see the original Hruby lens. He had been introduced to Dr. Hruby in Vienna in 1946 and was shown the lens which he had brought with him from Czechoslovakia. He supported Sir Stewart Duke-Elder's suggestion that it should always be called the Hruby lens.

Dr. Hruby, in reply, thanked the meeting for this very interesting discussion on his paper and said that he had understood most of the questions. The ophthalmoscope which they called the loupe ophthalmoscope was obtained by taking convex lenses of decreasing power starting with $+20$ D in the ordinary ophthalmoscope.

In reply to Sir Stewart Duke-Elder's observations, the connexion between the operculum of the tear and the hyaloid membrane remained until after the operation. It would be a very good thing if it were possible to separate it, but no instrument would cut away the vitreous, and so they had to apply especially careful diathermy needling to the base of the operculum. The operculum itself might stay detached—even for ever—or, occasionally, it might be torn out by the pulling action of the detached vitreous, and could be observed floating in the vitreous cavity.

The flashes which several speakers had mentioned occurred very often in old people and were due to vitreous detachment. Very often an elderly person would come forward saying that he had seen flashes and that there had been some obscuration of his vision. The question had been raised as to why this process occurred on the temporal side and never on the nasal side. His own teacher long ago gave him an explanation of that. The flashes were produced by the detached vitreous pulling on the peripheral retina, but the very peripheral retina on the temporal side was blind and on the nasal side it was not. Thus the flashes were experienced only at the temporal side.

A vitreous detachment could never go back. If he saw a case in which he had previously diagnosed vitreous detachment and afterwards found that it had apparently gone back he would say that he had made a mistake in his original diagnosis. Certain filamentous opacities in the retrolental space of the vitreous had been described by Vogt as remnants of embryonic blood vessels.

Air injection had been tried in his clinic in a few cases of retinal detachment recently. One of his colleagues brought back with him after a visit abroad the apparatus for the injection of air, but he himself had never carried out the operation so that he could not say anything about the changes which might develop. It opened up an interesting question and it would be useful to compare the results of the usual procedure with what happened in the vitreous after the injection of air.

In reply to Mr. Shapland, he liked to differentiate between changes in the framework of the vitreous or deposits in it, and opacities of the detached hyaloid membrane. When they started out to resect strips of the sclera, this procedure was restricted to more or less hopeless cases of retinal detachment. The results were poor at that time. He had had the idea of combining the usual diathermy treatment of retinal tears with the scleral resection in such cases, and since he had carried out that procedure the results had been better. The combined operation, however, lasted a long time, perhaps an hour and a half or sometimes longer. To make a scleral resection of the whole circumference of the globe might last three hours and was very difficult. Resection was done particularly in cases of shrinkage of the vitreous and of the retina, and any cases that had been operated on unsuccessfully. If there was a tear to be dealt with a combined operation was performed.

In the case of foreign bodies in which cornea and lens remained clear and the foreign body was behind the lens he would examine the condition with a slit lamp. He remembered one such case in which the sclera was penetrated but the hyaloid membrane was not broken and the foreign body was present in a tent-like sack of the subhyaloid space. In such a case he would bring it out by the posterior route.

In cases of dense opacities or hæmorrhages within the vitreous cavity vitreous withdrawal was advised as a therapeutic procedure. Sometimes a good method was tried once or twice and, as the results were not satisfactory, was abandoned undeservedly. He recalled a case in which a patient had diabetes and hypertension. The slit lamp showed quite clearly that the hæmorrhage was behind the detached vitreous. The blood was let out and the patient improved very much, but a few days later a new hæmorrhage developed. After a second withdrawal of vitreous another hæmorrhage occurred, and eventually the patient became blind by retinal detachment. That was exceptional and probably due to the fact that there was hypertension, but he was sure the procedure was a good one in appropriate cases and he would try it particularly in cases of subhyaloid hæmorrhages, and in cases in which the vitreous was liquefied. To deal with intra-vitreal opacities took a long time, the subhyaloid space was more quickly clarified by resorption.

In most cases of high myopia the vitreous became detached, and not only detached but also collapsed because the framework itself was destroyed.

Section of Dermatology

President—REGINALD T. BRAIN, M.D., F.R.C.P.

[*October* 15, 1953]

Plasma Cell Granuloma of Lips, Mouth and Larynx.—R. P. WARIN, M.R.C.P.

Mrs. L. M. P., aged 45, housewife.

Diagnosis.—Plasma cell granuloma of lips, mouth and larynx.

The condition began fifteen years ago, six months after the birth of a child. It has been less noticeable at times but never clear. Every few months there have been attacks of loss of voice, sore throat and cough.

Past history, family history and general health.—Nothing of note.

Examination.—The red margins of the lips are infiltrated by masses of raised granular cracked tissue. Similar tissue is seen over the tongue, on the posterior central area of the hard palate, on the faucial pillars, on the epiglottis and on the larynx (Fig. 1).

Investigations.—Blood: Cytology: normal limits. W.R. and Kahn test negative (1945 and 1953). Scrapings and swabs: no fungus elements seen. X-ray chest: nothing abnormal.

Biopsy from lip (Dr. A. L. Taylor).—The tissue shows nothing suggestive of neoplastic change but there is a very intense inflammatory reaction in which plasma cells are predominant.

Therapy.—A course of penicillin (procaine) 500,000 units b.d. for four weeks had no effect. A course of X-rays to the lips (total 900 r) caused a small but definite reduction of the raised areas.

Comment.—Cheilitis glandularis is characterized by the presence of deep pits and by the hypertrophied mucous glands which can be felt as nodules. In this patient these features are not apparent although, as the condition has been present for fifteen years, it is possible that they may have been obliterated by recurrent secondary sepsis.

FIG. 1.—Lips and tongue showing granulomatous infiltration.

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There is a condition described by Miescher (1945, 1951) as cheilitis granulomatosa which clinically seems very similar. However, the histology of Miescher's cases showed a picture similar in some ways to that of sarcoid whereas here the main feature is the plasma-cell infiltration.

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MIESCHER, G. (1945) *Dermatologica*, **91**, 57.
—— (1951) *Dermatologica*, **102**, 351.

Dr. G. Hodgson: We have had a similar case which we labelled "plasma cell granuloma". It responded extremely well to X-rays in large doses which have, however, produced some skin irradiation changes.

Dr. P. J. Hare: The histology reminds me of that in a case shown by Dr. W. N. Goldsmith at the International Congress in 1952. This was a man with peculiar lobulated swellings which practically obliterated the external auditory meatuses. He was given massive quantities of penicillin and also protracted X-ray therapy without benefit. Plasma-cell infiltrates in the skin are, of course, not uncommon, particularly on the face, and do not necessarily arise from the same cause.

Nævus Vascularis Reticularis (Two Cases).—R. T. BRAIN, M.D.

Case I.—P. G., girl, aged 13 years.

History.—The skin condition has been present since birth.

She was first seen at Great Ormond Street Hospital in 1940 at the age of 2 weeks. She showed an extensive mottled bluish-purple network of veins extending from the right ankle to the groin and up on to the flank. There are some dilated veins also along the right arm. Small ulcerated areas were present at birth on the right knee and shin. These healed in two to three months.

Family history.—Parents healthy; one sister, well.

The lesions on the right knee were treated from May 1947 to February 1948 with 8 paintings of thorium X solution, 2,000 Electrostatic Units per c.c. No improvement was observed.

Examination.—There is still a mottled network of enlarged venules over the right arm and leg. W.R. negative.

Case II.—R. M., aged 9 weeks.

History.—Skin condition present since birth. Parturition normal. General health good.

Family history.—Mother had thyrotoxicosis for four years treated with thiouracil before pregnancy began. Toxæmia of pregnancy. Mother has old healed pulmonary tuberculosis. 2 maternal uncles died of tuberculosis. Father had asthma.

Examination.—Well-proportioned baby. Body symmetrical (age 9 weeks). Anterior fontanelle patent.

Skin: Right temple shows slightly depressed bluish-red macules. Some coarse venules over right parietal area.

Face shows a reticulate erythema.

Behind the right ear is a bluish macule 1 in. diameter of irregular shape; it has a central area of pale depressed hairless skin in the centre.

Right side of the trunk, arm and leg to a greater degree than the left shows a reticular pattern of pink to purple discoloration with telangiectasia at the edge and atrophy in the centre, allowing larger venules to be seen through the thinned epidermis.

Right hand and ankle show some superficial erosions and crusts.

On the right thigh and leg are some more deeply depressed areas in which the whole skin thickness is atrophied. There is no muscle involvement. The nails are normal.

Histology (from L. scapular area) (Dr. M. Bodian).—There is a hæmangiomatous malformation in the deep collagenous subcutaneous tissue of the central portion of the specimen; the fat tissue, corium and epidermis are atrophic. The angioma consists partly of unexpanded blood vessels, and there is some extension of the lesion into the subcutaneous fat.

Comment.—The two cases shown, at first sight presented the purplish reticular mottling of the skin which appeared to be an unduly conspicuous variety of livedo reticularis, or livedo racemosa if we restrict the latter term to the inflammatory disorders of the cutaneous vessels. However, it is generally accepted that the milder cases are due to functional disturbances most commonly seen in a somewhat debilitated child in cold weather: they may more simply be described as marbled skin or cutis marmorata.

As the condition persisted in the first patient (P. G.) there seemed to be no doubt that we were dealing with a congenital mesodermal abnormality, mainly affecting the blood vessels. In the second case, this was some more obvious from the beginning; the abnormal vessels were more conspicuous and there were some dystrophic changes in the skin in which the vessels lay.

Few examples of this condition appear to have been reported in the literature, but an extensive one was described by van Lohuizen (1922) illustrated with black and white and one coloured photograph. He described the condition as cutis marmorata telangiectatica congenita and described the curiously variegated dark bluish, red-flecked, marmorated pattern which involved most of the body surface, except for the narrow band in the mid-line of the chest and abdomen. The nose, lips, ears, genitals, palms, soles and mucous membranes were not affected. The condition was noted at birth and there was some improvement in the first two years especially in the face. The child was otherwise apparently normally developed and the confinement normal, and there was no other case reported in the family. The W.R. was negative.

It was noted that over some of the dark bluish-red network, the lines of which were 1 to 3 mm. wide, the surface was depressed. The lesions had the appearance of vascular nævi, and this was supported by the presence of a number of conspicuously dilated tortuous veins. The histology showed an increase of pigment in the basal cells. There were many dilated blood vessels of capillary structure in the cutis, some of the vessels had a thickened wall and formed lacunæ, but there was no infiltration about the vessels. A somewhat similar, but not so extensive, condition was reported by van West and, in this case also, some of the discoloured areas were partly depressed.

A somewhat similar picture may be produced by endarteritis or endophlebitis of some of the deeper vessels and Ehrmann (1907) described as livedo racemosa the consequence of damage to the vessels by syphilis. Others have described similar changes which they related to tuberculosis or exposure to cold.

Ebert (1927) described a case of livedo in a woman aged 33 associated with tuberculides of Bazin's type, acrocyanosis and incipient Raynaud's disease. Livedo reticularis was preceded by cutis marmorata which served as a pattern and predisposing cause.

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EHRMANN, S. (1907) *Wien. med. Wschr.*, **57**, 777.
VAN LOHUIZEN, C. H. J. (1922) *Acta derm. venereol.*, **3**, 202.

Dr. R. D. Sweet: I saw a baby about eighteen months ago very similar to the girl shown this afternoon. The distribution was generalized, but at 1 year the lesions had almost disappeared.

Dr. Theresa Kindler: Ehrmann, who found that 15 of his 17 patients were syphilitic, thought at first that livedo racemosa was a manifestation of tertiary syphilis, occurring in the second or third decade after infection. He held the view that deposits of spirochætes in the endothelia of the deep vessels provoked an obliterating endarteritis which led to subsequent stasis in and dilatation of the capillaries. Other authors, however, found the condition in tuberculosis, cardiac and circulatory disease, alcoholism, or provoked by frostbite and frequent exposure to cold. Ehrmann himself later modified his opinion in that he said that various noxæ and systemic disease may cause similar vascular changes. The disease is, however, still referred to as tertiary syphilis in recent editions of various textbooks.

Dr. P. J. Hare: A similar reticular pattern was described by Dr. Freudenthal following intra-arterial injection of bismuth. This might lend support to the notion of an endarteritis having occurred in the present case.

REFERENCE

FREUDENTHAL, W. (1924) *Arch. Derm. Syph.*, Berlin, **147**, 155.

Dr. B. C. Tate: I am not sure that these are the same condition; I should regard them as somewhat different. On the strength of one case of my own I should give a much better prognosis for the baby where I think there will be a much greater degree of recovery than in the bigger girl.

The following cases were also shown:

Mongol Spot.—Dr. J. E. M. WIGLEY.

Bullous Pemphigoid with Dystrophic Changes.—Dr. R. H. MARTEN for Dr. F. RAY BETTLEY.

Case for Diagnosis. ? Pityriasis Lichenoides et Varioliformis Acuta (Habermann).—Dr. I. MARTIN-SCOTT.

Case for Diagnosis. ? Pityriasis Lichenoides et Varioliformis.—Surgeon Lieutenant-Commander R. SCUTT.

Idiopathic Œdema.—Dr. M. FEIWEL.

Case for Diagnosis. Dermatitis Artefacta.—Dr. N. A. THORNE for Dr. BRIAN RUSSELL.

(1) Granuloma Annulare. (2) Vitiligo Treated with Meladinine.—Dr. C. D. CALNAN.

[These cases may be published later in the *British Journal of Dermatology*.]

[*November* 19, 1953]

Porokeratosis Striata (Nékam).—R. H. MEARA, M.R.C.P. (for J. E. M. WIGLEY, F.R.C.P.).

K. P., male, aged 27.

History.—The patient has noticed the slow development of the present lesions during the last twenty months. They give rise to no symptoms, and the patient has no knowledge of any similar affection occurring in his family.

On examination.—On the dorsa and soles of both feet and spreading up to the ankles are tiny pinkish macules, about 2 mm. across, each with a central horny raised plug. These can readily be removed, leaving shallow pits. The anterior aspects of the wrists are similarly, though slightly, affected and there are a few lesions on the flexor aspects of the forearms.

Histology (Dr. H. Haber).—A lesion of the ankle was excised. "In the centre of the lesion there is a parakeratotic rivet-like plug, probably filling out a sweat duct. The upper corium shows a mild round-cell infiltration."

Comment.—This patient appears in some respects to be similar to the one described by Kaposi (1895). She was seen again twenty-six years later by Nékam (1938). Kaposi named this condition "Lichen Ruber Verrucosus et Reticularis" and considered that it was a variant of Pityriasis Rubra Pilaris. Nékam described hyperkeratosis of the mouths of the sweat ducts and suggested the name "Porokeratosis Striata Lichenöides".

The case presented here does not show the linear and striate verrucose lesions described by Kaposi and Nékam but only the punctate keratotic lesions probably related to the openings of the sweat ducts.

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KAPOSI, M. (1895) *Arch. Derm. Syph.*, Wien., **31**, 11.
NÉKAM, L. (1938) *Pr. méd.*, **51**, 1000.

Lymphangiosarcoma in Postmastectomy Lymphœdema (Stewart-Treves Syndrome).—S. P. HALL-SMITH, M.D., M.R.C.P., and H. HABER, M.D.

Mrs. E. W., aged 72.

History.—Two years ago she developed small red spot over medial border left upper arm which has gradually enlarged to its present size. Her left arm has been swollen and œdematous since the operation in 1949, and she states that her left side of neck and left face are also slightly swollen.

Past history.—August 1949, left radical mastectomy by Mr. J. Kerr, Royal East Sussex Hospital, for carcinoma of left breast. This was followed by 15 applications of deep X-ray therapy. She suffered a severe reaction of the neck, shoulders and arm following the radiotherapy.

January 1952, right radical mastectomy.

On examination.—Indurated dark red lesion, slightly raised 4½ cm. × 3 cm., set in middle third of medial border of left upper arm—a few tiny satellite lesions have recently appeared. The immediate surrounding skin is unaffected by X-ray telangiectasia.

Left arm swollen compared with right, and forearm and hand œdematous. Diameter 31½ cm. compared with 25 cm. on right side.

Marked X-ray telangiectasia over left neck and shoulder region and left upper arm (Fig. 1).

FIG. 1.—Showing angiosarcoma arising from lymphœdematous left arm, and X-ray atrophy and telangiectasia over shoulder.
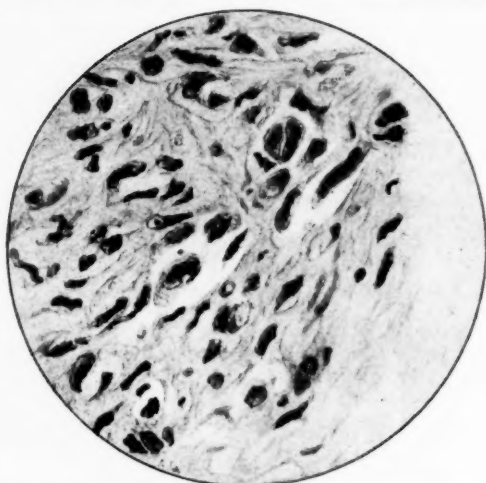
FIG. 2.—There are numerous spindle-shaped cells with dark hyperchromatic nuclei showing vasoformative properties. × 500.

FIG. 3.—To illustrate a capillary lined by giant endothelial cells with large hyperchromatic nuclei. × 500.

FIGS. 2 and 3; Micro-drawings by Miss A. Gretener.
Institute of Dermatology.

Histopathology.—Sections from the tumours in left and right breasts (Dr. J. McMurray): Removed at interval of three years these both show adenocarcinoma. The pattern suggests origin from duct epithelium. No tumour is present in the lymph nodes sectioned.

Section from tumour left upper arm (Dr. H. Haber): There are several foci of a tumour consisting of numerous bizarre-shaped cells containing hyperchromatic nuclei, with a tendency to form vascular lumina. One or two mitotic figures could also be seen in the section. Somehow this feature combined with extravasation simulates the appearance of a Kaposi's sarcoma. Blood pigment is absent (Figs. 2, 3).

Summary.—This is a malignant tumour with vasoformative properties. In view of the history of the case it could be regarded as a lymphangiosarcoma.

X-ray of spine.—July 1952, shows marked osteoporosis and collapsed vertebræ aggravated by osteoarthritis. No evidence of secondary change attributable to her carcinoma of breast.

Comment.—Stewart and Treves (1948), Ferraro (1950) and Jessner *et al.* (1952) in their reports comment on the following points:

All cases so far recorded occurred in women 46–68 years old. The interval between the mastectomy and the onset of angioblastic sarcoma in these 8 cases ranged from 6–24 years. As some swelling of the arm is to be expected in 70% of women undergoing radical mastectomy the condition may be of more than academic interest and in the past it may have been confused with Kaposi's sarcoma or recurrent mammary cancer. All observers agree that radiotherapy is ineffective and that inter-scapulothoracic amputation is indicated.

The presence of a systemic carcinogenic factor has been postulated by Stewart and Treves, which, under certain favourable conditions, e.g. lymphœdema, produces a lymphangiosarcoma. Jessner, Zak and Rein mention the observation of Toolan and Kidd, that mammary carcinoma cells which had sojourned in immune mice produced sarcoma-like pictures including reticulin formation, and remark on the possible connexion between this observation and the Stewart-Treves syndrome.

Our case differs from previously reported cases in that the time interval between her left radical mastectomy and the onset of the angioblastic sarcoma was only two years, and the patient herself was two years older (70) than any other recorded case. She cannot date accurately the commencement of the lesion on the lymphœdematous arm though she thinks there was some sign of it before her right radical mastectomy in January 1952.

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FERRARO, L. R. (1950) *Cancer, N.Y.*, **3**, 511.
JESSNER, M., ZAK, F. G., and REIN, C. R. (1952) *Arch. Derm. Syph., Chicago*, **65**, 123.
STEWART, F. W., and TREVES, N. (1948) *Cancer, N.Y.*, **1**, 64.

Dr. Daphne Anderson: I have seen one case of this condition but instead of one large tumour there were many small tumours on the arm, more like the case described by Stewart and Treves (1948, *Cancer, N.Y.*, **1**, 64). I would like to question the point of treatment by amputation. When this gross œdema of the arm following mastectomy is found there is usually a residual tumour present either in the axilla or in the supra-clavicular region. More harm may be caused by amputation than by leaving it alone. When it is said that 70% of cases have œdema of the arm I would say that a large percentage have minor degrees of œdema after removal of the lymphatics and these gross degrees occur in patients with residual tumours.

Dr. P. M. Inman: Is it an essential feature of the syndrome that they must have received deep X-ray therapy? Is the onset of this tumour related to the X-ray therapy rather than to the œdema? Has this ever occurred in a person not receiving X-ray therapy?
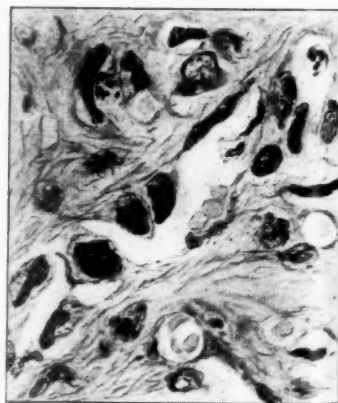
Gentele (1951) reports 11 cases of fibrosarcomatous tumours occurring in radioatrophic skin. He notes that "tumours similar to these have been found to be of epithelial nature, a kind of spindle-cell carcinoma". Although his cases had not angiosarcomatous elements a sarcomatous appearance in X-ray damaged skin may be due to a carcinomatous tumour.

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GENTELE, H. (1951) *Acta derm.-venereol., Stockh.*, **31**, Suppl. 27, 133.

Dr. F. Ray Bettley: I understand from Mr. R. S. Handley that the œdema is by no means always an indication of persistent or recurrent growth but is often a direct complication of the operation. Mr. Handley has been treating them with hyaluronidase injections apparently with good results. A partial relapse occurs after the first treatment; a second series of injections results in further improvement, and Mr. Handley's impression is that eventually some permanent improvement may result. I do not suppose that Mr. Handley is ready for the results to be published but I mention the treatment because it possibly offers an alternative treatment in this case. If in this patient the œdema can be relieved it may be that the lymphangiosarcoma is also reversible.

Scleredema (Buschke).—C. D. CALNAN, M.B.

Mrs. E. C., aged 37.

History.—7.7.53: She developed an acute sore throat with fever, general malaise, aches and pains: she was confined to bed for five days.

7.8.53: Swelling of her face began with hardening of skin of face, neck, shoulders and upper chest. Movements of all joints in these areas were greatly restricted.

No weakness or constitutional disturbance.

On examination.—The skin of the upper part of the body is hardened into one continuous solid mass. The face is swollen. The swelling extends to the upper abdomen and to the wrists; the hands are entirely spared. The skin is not discoloured and is of normal appearance. There is no pitting œdema. The whole head, including the scalp and eyelids, is involved. There is no loss of muscle power.

Investigation.—Creatine excretion (two tests): 370 mg. per twenty-four hours; 174 mg. per twenty-four hours.

Histology (Dr. H. Haber).—The epidermis is normal. The corium shows a marked widening of intercellular spaces and some scattered inflammatory cells.

Histochemical tests were performed by Dr. A. G. E. Pearse. He reports: "The ground component is a labile water-soluble mucopolysaccharide quickly removed by hyaluronidase. In paraffin section, Alcian Blue (specific for connective tissue masses in this case) shows that very little remains. The collagen should be red in KRAG and red in PICMAL which, largely, it is not; brown in reticulin stain, which it is. It is obviously abnormal (deficient in basic groups) chemically and less obviously physically, since the reticulum is almost normal, except for dark staining of some of the upper masses. With acetone fixation, the collagen fibres have shrunk and broken—this is pretty demonstration of weakness in some form. The elastica is peculiar and possibly excessive. It has the appearance of a cross between myxœdema and scleroderma, but is not absolutely like either. (Enzyme studies were not helpful in diagnosis.)

Treatment.—Cortisone 150 mg. per day for three weeks produced no change. Hyaluronidase iontophoresis also failed to alter the condition.

Details of the stains used are:

> KRAG = Kiton Red Almond Green (Lendrum, 1949).
> PICMAL = Picro-Mallory (McFarlane, 1944).
> Alcian Blue (Pearse, 1953).

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LENDRUM, A. C. (1949) *J. Path. Bact.*, **61**, 443.
McFARLANE, D. (1944) *Stain Tech.*, **19**, 29.
PEARSE, A. G. E. (1953) Histochemistry. London; p. 151.

Dr. G. B. Dowling: I recently looked up some literature on this disease and found some American cases reported as having persisted for a number of years, even ten years or more. These reports suggest that the prognosis in time is not always as good as it is perhaps generally believed to be, that is, residual hardness may persist for many years.

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LEINWAND, I. (1951) *Ann. intern. Med.*, **34**, 226.
VALLEE, B. L. (1946) *New Engl. J. Med.*, **235**, 207.

Dr. J. Sommerville: I had a similar case, perhaps not so marked, three years ago, and it cleared up in about fifteen months.

Dr. C. H. Whittle: What has been the experience of members using hyaluronidase? We have used it in cases of chronic lymphœdema, so far without success.

Dr. F. Ray Bettley: Dr. Hicks and I showed a case of this type some years ago (1949, *Brit. J. Derm.*, **61**, 294) and the diagnosis was then questioned chiefly on the ground that it was going on too long. My patient had then had it for nine or ten months and was showing little sign of recovery.

Dr. I. S. Hodgson-Jones: How were the cases which Dr. Whittle treated unsuccessfully given the treatment? The molecule is very large and it will travel between electric poles only very slowly so that it takes some hours to get well into the skin. I have been unable to confirm, experimentally, that effective amounts of hyaluronidase can be introduced into the skin by usual iontophoretic technique.

Dr. Whittle: We have only had very few cases but we used an injection locally without success and then we changed over to the more popular ionization, again with no success.

Dr. N. A. Thorne: At the London Hospital we have tried treating three cases of scleroderma with hyaluronidase, both by iontophoresis, using the method described by Popkin, and by local intralesional injections of hyaluronidase. Both methods have failed to cause any obvious clinical improvement.

The following cases were also shown:

Pyodermite Végétante.—Dr. H. J. WALLACE.

> (This case will be published in the *Proceedings* at a later date.)

Lymphoma of Mycosis Fungoides Type Treated with Mepacrine (Three Cases).—Dr. C. H. WHITTLE and Dr. J. L. MOFFATT.

Secondary Carcinoma of the Skin.—Dr. W. G. TILLMAN.

An Unusual Case of Necrobiosis.—Dr. BRIAN RUSSELL and Dr. H. HABER.

Case for Diagnosis.—Dr. PETER BORRIE.

Nævoxanthoendothelioma.—Dr. E. LIPMAN COHEN.

(1) Scleroderma—en Coup de Sabre. (2) Reiter's Disease.—Dr. J. B. LYON.

> (These cases may be published later in the *British Journal of Dermatology*.)

Section of Medicine

President—Professor Sir HENRY COHEN, M.D., D.Sc., LL.D., F.R.C.P.

[*November* 24, 1953]

DISCUSSION: THE USE AND ABUSE OF REST AS A THERAPEUTIC MEASURE

Dr. G. E. Beaumont: *The Use of Rest as a Therapeutic Measure*

The dangers of rest are well known; Mark Twain points out how many more people die in their beds than when travelling by train. "Don't take any more chances on those beds", he says, "the rail-roads are good enough for me."

There is, however, the other side to the question. I like my bed. I like it when I am well, and I like it still more when I am ill. In order to derive the full benefit of rest during illness, not only the body, but also the mind must be relaxed. In long and serious illnesses a state of mental tranquillity is frequently observed. One of my house physicians at Brompton, who had previously been a house physician at Middlesex, remarked to me how impressed he had been by the fact that the patients at Brompton, who had been in bed for several months, seldom made any complaints, whereas those confined to their beds in a general hospital, for only comparatively short periods, were often full of melancholy moanings.

If an illness is sufficiently long and sufficiently disabling, the patient's mind often becomes dulled and free from thought, and so, automatically, it is at rest.

It is equally true, in my experience, that those who do not achieve mental rest and resignation during a long illness, will take longer in recovering, and are more prone to setbacks, than are their more tranquil brethren.

There is another feature in the life of the invalid confined to bed, which, by disturbing his rest, may retard the progress of his recovery. I refer to visitors.

There is no doubt that visitors can be, and often are, extremely exhausting for the patient, especially during the early stages of convalescence.

Poliomyelitis.—Physical rest is a necessity in the treatment of the majority of acute illnesses, and of vital importance in the treatment of many a prolonged one. Attention has recently been drawn to the value of rest in the early stages of poliomyelitis; for the patient who takes to his bed at the onset of the disease is far less likely to develop paralysis than is the sufferer who keeps about during the early stages. The housewife, who stays at her work, is especially liable to suffer in this respect.

Pulmonary tuberculosis.—Here, rest is of paramount importance—rest of the mind but, above all, rest of the body. The evil effect of exercise in tuberculosis is shown by the rise in temperature which will follow a moderate walk, if the disease is active.

When I first worked at Brompton as a house physician we paid great attention to the value of prolonged periods of rest in bed. With prolonged periods of rest in bed, sometimes for a year, as good or better results were seen in some cases of advanced and extensive tuberculosis as can now be obtained by the use of antibiotics and chemotherapy.

After the first world war artificial pneumothorax became generally used in suitable cases, and this proved an enormous step forward in curing the diseased lung by rest alone.

The first thoracoplasty performed at Brompton was, I believe, on one of my patients. Since then many modifications have been made in the operation.

Even with the best results a less perfect degree of collapse of the lung is obtained with a thoracoplasty than with a good pneumothorax. But a disturbing feature in the treatment of pulmonary tuberculosis, as the result of these extensive operations on the chest, has been the introduction of all kinds of limb and body exercises.

There is always much more of the lungs affected by tuberculosis than is shown by X-ray examination, and to subject such lungs to forced movements by breathing exercises involves the risk of activating these latent foci. It is possible that the spread of tuberculosis in the other lung, which sometimes follows thoracoplasty, is due to the post-operative exercises, rather than to an inhalation or broncho-genic transfer of infected material.

It may, of course, be argued that these exercises would not be universally practised if this risk were a real one. I suspect that the surgeons themselves are not too happy about this procedure, for when the patient has been put through this course of therapeutic gymnastics, and when he has, as they say, "cleared his chest", he is put back to bed rest for a further period of weeks or months.

Rest and be saved is the motto which should be put in each patient's room.

MAR.

Sciatica.—Until towards the end of the 1930s, sciatica was usually treated by various forms of physiotherapy—passive movements, stretching the nerve, Vichy douche, Aix douche, massage under water and on the slab, foam baths, mud baths, ionization, infra-red, radiant heat, diathermy, or short-wave therapy.

If the patient is subjected to each and all of these the sciatica, as is only to be expected, becomes more and more acute. The patient arrives at the spa ambulant, he returns recumbent.

It seems to me to be good sense to rest an acutely inflamed or irritated structure, and, when later it was discovered, or thought to be discovered, that many cases of sciatica were due to a prolapsed disc, the enthusiasm for the various forms of treatment I have enumerated, curiously waned, and the wisdom of giving rest to the back and leg was appreciated.

Rheumatoid arthritis.—How much harm has been done and how much suffering caused by physical treatments? In subdeltoid bursitis, for instance, which may occur as a part of infective arthritis, the treatment often recommended is active and passive movement, under the deluded idea that if the joint is not exercised and moved adhesions will form. Actually the converse is true. The passive movements cause excruciating agony, the patient nearly swoons, and rest or sleep at night is prevented by the subsequent increase in pain. The temperature rises, and adhesions later form, which prevent full movement of the joint.

There is one exception I would make to the use of physical treatment, and that is for deep X-rays. These, combined with rest for the joint, give the best results for subdeltoid bursitis.

In the treatment of rheumatoid arthritis rest in bed for several months is of the greatest importance. The patient is often unwilling to take to his bed—he struggles on with his work as one joint after another becomes affected. There is never a let-up in the pain, which continues relentlessly by day and by night, unless the joints are immobilized.

After having his septic foci removed, the patient may be sent by his doctor, in conformity with popular opinion, to a spa for treatment. He is there subjected to massage, to colonic washouts, with the beneficent waters in which the spa specializes, to baths, to water squirted under high pressure from a wide-bored hose-pipe on to his swollen wrists, as he flounders helplessly in a deep pool. After each treatment the wrists become more swollen and painful. The effort of undressing and dressing, when practically every joint in the body, except the spine and hips, is involved, is fatiguing in the extreme. The patient is exhausted by the profuse sweating which takes place when he is "packed up" in blankets after the bath, he loses weight and becomes progressively weaker and more despondent. Eventually the doctor tells him that his case is unsuitable for spa treatment, or that his heart is too weak, and advises him to go home, go to bed, and stay there for several months.

It is only after taking to bed completely after several months of partial activity and of various forms of physiotherapy that the patient begins to improve.

Rest on splints is very important for the affected joints in rheumatoid arthritis, both in the acute and subacute stages. Exercise is followed by swelling, increase of pain, rise of temperature and further limitation of movement.

The splints should be removed for a few hours each day, during which the patient moves the joints gently without causing a lasting increase in pain.

In my hospital work I have found that it may be necessary to keep a patient with rheumatoid arthritis in bed in hospital for periods up to eighteen months. I have seen excellent results follow such treatment, the patient being able to return to his work, with full movements in all joints.

And, in conclusion, we are told now that exercise and worry result in obesity. If, therefore, you wish to get thin, go to bed and let your mind be at rest.

Professor C. A. Wells: *Rest—Its Use and Abuse*

In a changing world we must adapt our ideas to changing circumstances. For example I might mention the role of sympathectomy in angina of effort. This operation abolishes or modifies the *pain* which calls for rest—or does it?

In tuberculosis, the introduction of effective chemotherapy (in its broadest sense) has tended to emphasize the importance of rest and the sanatorium regime, but this is partly because of the need to have patients under observation whilst the rather tricky therapeutic regime is carried out. Local rest in bone and joint tuberculosis, introduced by Hugh Owen Thomas remains substantially unchanged and some form of mechanical restraint is the rule. However, Rollier, in Leysin, who has given sun-worship the fervour of an orthodox religion, nurses his spinal caries lying on their faces *without* mechanical restraint. This leads to striking development of the erector spinæ muscles, giving active support to the diseased area in optimal position. I have never understood why this method which subtly combines rest with exercise, has not gained more general acceptance. I regularly recommend it for the prophylaxis and treatment of prolapsed disc—but as I seldom see these cases, nobody takes much notice!

In orthopædic practice the treatment of fractures and sprains aims at precisely this combination of rest with exercise. A fractured scaphoid is *rested* by complete fixation of the wrist in dorsiflexion:

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but he fingers move freely and the tendons play busily over the wrist-joint. Months of fixation in plaster cause no disability. If the fingers are too straight in the plaster or cannot move well, disaster may result; the hand may be so "frozen" as never again to be useful.

The care of fracture of the spine with paraplegia.—Frank Holdsworth has shown that in the majority of such cases the nervous lesion is in the cauda equina which can recover if rested and not subjected to repeated trauma. Active intervention for the fixation of the fracture dislocation by plates clamped together across the spinous processes protects the cauda equina. It also enables one to rest the pressure points of the skin by two-hourly movement of the patient from side to side. Thus by the most vigorous treatment, true local rest is assured. Suitable cases (the majority), adequately treated, develop no sores and can leave hospital in less than a year with a great deal of recovery.

I well remember, three years ago, asking Dr. L. Guttmann of the Stoke Mandeville Spinal Centre to come to Liverpool to see a patient about whom I had been consulted. The man was dying from enormous pressure sores, having barely escaped death from peritonitis. Dr. Guttmann said he must be turned hourly or, at least, two-hourly—both day and night—regardless of whether he was sleeping or not. We carried out these instructions and other suggestions and the patient recovered. We had great difficulty, however, in justifying to both him and his family, the need for this apparently ruthless interruption of his proper "rest". This is another example of the difficulty we may have in distinguishing between activity (in this case general) and rest (in this case local to the necrotic areas).

Tuberculosis.—In the treatment of pulmonary disease in recent years there has been a shift towards excision of the whole or part of a lung. For a long time however, rest, through what is broadly termed collapse therapy, has held pride of place in surgical treatment and probably still does. The results have certainly been well worth while and afford yet another example of local rest in surgical practice. The inability to afford rest to the kidney has been held to be one of the main reasons why renal tuberculosis, once established, never heals. Here again, resection is being employed more and more.

Possibly the best example of the discarding of a firmly established technique of rest is the throwing overboard of the Fowler position. This time-honoured feature of after-treatment was already on its way out before the antibiotics lessened the cogency of the reasoning on which it was based, namely the localization of peritonitis to the pelvis. The fear of deep venous thrombosis was probably the most powerful argument against the Fowler position. The comfortable propping up in bed of our nursing-home patients was probably the biggest single cause of the high incidence of pulmonary embolism in private surgical practice. For twenty years now I have used a post-operative regime of posture and exercises designed to lessen the incidence of this dreaded accident. From the day of operation, my patients are, for ten minutes daily, placed flat, without a pillow, and preferably with the foot of the bed raised. Active and passive movement, especially of the legs and feet and deep breathing under the supervision of the physiotherapist are carried out. This activity should serve to empty the veins and lessen the risk of thrombosis and embolism. I believe it does so.

Early ambulation.—In my own practice, patients are usually got up from bed the day following operation, in all but the very biggest procedures and often even in these also. The old bed-pan gives way to the thunder box—unnecessary invalidism is avoided and, at the end of ten to fourteen days, the convalescent walks out, dressed and carrying his own suit-case—this at a moment at which, a few years back, the more daring of us were wont to allow our patients to sit up in a chair for the first time. The avoidance of the invalidism of bedfastness is invaluable and is a direct negation of the old policy of prolonged rest. Ambulation alone, however, does not prevent thrombosis and embolism. The slow movement of dependent legs in the first day or two is not enough to prevent stasis and thrombosis. Bed exercises such as I have described are still necessary.

Very recently a new approach through anæsthesia is opening up a new prospect. By giving the new drug, chlorpromazine hydrochloride, which puts the heat-regulating mechanism out of action, we are able to cool the body down with ice-packs and exposure to a rectal temperature of 30° C. or less. This effect comes into operation before the anæsthetic is begun and continues for at least twenty-four hours after the patient is returned to the ward from the theatre. There is a state of profoundly diminished sensitivity surpassing sleep and subsequent amnesia, such that when he awakens it may be difficult to convince the patient that he has had his operation, even though this may have been a mara-thon procedure occupying several hours. During the period of hibernation (so-called) the consumption of oxygen and of anæsthetic drugs is remarkably low, and the blood pressure falls to the region of 60 mm.Hg systolic. Despite the low pressure and small oxygen consumption, at these low temperatures cerebral and renal damage do not occur; anæmia is well tolerated as also is further severe blood loss. At the lowest temperatures, in cardiac surgery, the circulation may be completely arrested for several minutes without serious consequences. In this state of almost suspended animation all the mani-festations of "shock" seem to be dulled. The coagulability of the blood is lowered, hæmorrhage is a little difficult to control and, presumably, the risk of thrombosis is greatly lowered. It is this last point which led me to mention this subject, but it does also serve to illustrate the way in which we may be swung from the practices of a lifetime—preservation of warmth, maintenance of blood pressure and so forth—to exactly contrary procedures.

Some preliminary observations which one of my research students has made on the electrolyte levels, during and after operation in hibernation, suggest that the shifts of sodium and potassium ordinarily observed in relation to surgery, may be modified. Of course, one of the known features of the post-operative period is excessive protein breakdown. Oddly enough this occurs at a comparable speed if one merely goes to bed without having an operation! The question arises: "Is bed a stressor?" I am interested in this because another young man in my Department is studying the application of the general adaptation syndrome of Hans Selye to the phenomena observed after surgical procedure and seeks to relate the retention of sodium and other observable changes to increased cortical activity in response to surgery. If this relationship can be established and if it can be shown that in hibernation the stress response is minimal, we may have taken quite a step forward towards explaining the mechanism of a whole series of events intimately related to the response of the body not only to trauma but also to rest and activity.

To summarize: For the surgeon, rest must be subdivided into local and general. Whatever may be the need for the local variety, general rest is fraught with dangers for both the surgeon and his patient and no longer has the sanction of universal custom. The early restoration of normal general activity is an aim in itself and, by and large, an important aid to convalescence,

Group Captain C. J. S. O'Malley, C.B.E., M.B., B.S.: *Exercise and Relaxation*

My approach to this subject is conditioned by some ten years' experience of working in Medical Rehabilitation Centres. At these Centres an endeavour has been made to produce a balanced programme of exercise and relaxation; an appreciation of the total situation governs the regime.

The majority of this experience has been gained in the Royal Air Force Medical Rehabilitation Units, and if I may, within the precincts of this learned Society, lapse into Air Force slang, this propaganda rhyme, freely exhibited in all Royal Air Force Centres would appear to be apt—"Intermittent Rest and Work makes a strong and healthy Erk"—the last strange word being Royal Air Force Slang for "Aircraftsman".

Our endeavours in these Centres, and in the Centre at which I am working at the moment, have been to overcome the apathy and ennui of the sick and injured man. In the past, when medicine had few specific treatments, rest was the sovereign remedy, and even now we are greatly influenced both by John Hilton's "Rest and Pain" and through Hugh Owen Thomas' teachings. In these days of chemotherapy, we do not need excessive rest to overcome infections. Many of the problems seen in a Rehabilitation Centre are caused by over-indulgence in rest.

I shall take the problem of the treatment of anterior poliomyelitis as an example of what I mean by "good timing" and a balanced programme. Seddon has stated that the treatment of poliomyelitis can be described by the activities of three types of therapeutists:

(1) *The Fixers*, i.e. those who indulge in excessive static splints, and in the words of Ritchie Russell, "believe that paretic muscles should be rested in a relaxed posture throughout most of the day, and that in severe cases, the gradual return of freedom of movement should be spread over a period of eighteen months."

(2) *The Floggers*, i.e. those who believe that cases of poliomyelitis should be exercised to the point of fatigue.

(3) Those who indulge in Festina Lente—he himself subscribes to this "Make haste slowly approach."

In my opinion, poliomyelitis cases, three months after the onset of infection, can be exercised to a very much greater extent than modern teaching suggests.

Seddon is also of the opinion that there is no great recovery of function after six months. However, it is my contention that functional recovery in a determined patient can be greatly improved by an active regime in a Rehabilitation Centre.

I have had cases at Garston Manor Rehabilitation Centre who have been unable to manage our stairs. We have purposely made no provision for a lift. These stairs have been climbed within three weeks of coming to the Centre. One case, on admittance, climbed these stairs in one hour, and left three months later, climbing these same stairs in six minutes. This improvement in function occurred three years after the onset of poliomyelitis. Is this recovery of function due to regular exercises causing hypertrophy of the remaining muscle fibres in the paretic muscles?

In our experience the more determined the patient is, the better the results, and the balanced regime should be put into practice three months after the onset of the infection. Perhaps our experience with the relatively minor disability of the internal derangement of the knee-joint might illustrate the importance of active exercises following the operation for meniscectomy.

Before the war, and even now, we find many patients not working for some twelve weeks after operation. During the war, in the Royal Air Force Centres, our best results were the return to duty in six to eight weeks, provided the patient was sent to the Centre fourteen days after operation. In my present Centre the average time of 77 cases of meniscectomy is twenty-eight days for return to full work. This includes cases which went back to work as agricultural labourers. These cases came from a hospital which sent their patients three to five days after operation, before their sutures were removed.

The simple operation of herniotomy, also illustrates this point. It is not so very long ago that these cases were kept in bed for three weeks. My last 23 cases have been sent to the Centre seven days after operation, and have returned to full work in twenty-one days after operation. These results have been obtained by a balanced regime of muscle development and relaxation, and the careful appreciation of timing, resisted exercises and avoidance of fatigue.

Failure to start the patient early on often results in stagnation and prolongation of convalescence.

The modern concept of a dynamic approach to convalescence has made enormous strides in the reduction of the duration of a disability, though the average convalescent home still has little appreciation of the importance of a balance between relaxation and exercise.

Progressive relaxation.—The importance of the quiet hour and the hygiene of the quiet mind. The problem of rehabilitation is the treatment of people. Patients should be studied as a whole, and their many personal problems and motivations resolved.

We try to make the patient perform the appropriate movement in a different way all day—his movements being balanced by the spacing of periods of relaxation.

In our Centre patients work in half-hourly periods from 9–12 noon and 2–5 p.m. with a half-hour break mid-morning and mid-afternoon, these break periods being eased by the provision of light refreshments. The half-hourly periods are made up of twenty minutes exercise and ten minutes relaxation.

The direct attack, using traditional physiotherapy and remedial exercises, is balanced by the indirect approach of remedial games, and what we prefer to term work-therapy.

The centre is divorced from the hospital atmosphere of disability. Ability is stressed, and endeavour fostered. It is sometimes difficult to maintain this hopeful attitude in a hospital, where inevitably patients sometimes die, and sometimes get worse. It is interesting to note that Hippocrates stressed the triad of therapy: (1) The gymnasium. (2) Hydrotherapy. (3) A change of climate or environment.

It would seem that he appreciated the importance of exercise in the stage of recovery.

Asthma and chronic bronchitis.—Patients are sent to the Centre when the acute infection has been controlled by specific treatment. A programme of relaxation, breathing exercises and gradual activity is initiated. An endeavour is made to control the "panic reactions" of these patients, by teaching them to relax, firstly lying down, and then progressively, sitting, standing, walking and eventually running. We believe that the approach to this problem will be more rewarding than the policy of "Rest and yet more Rest".

Rheumatoid arthritis.—Apposition of the thumb and first digit is essential for all aspects of daily living. How often have we seen that this movement is the only efficient movement left in a case of rheumatoid arthritis.

I believe, if we could produce painless movement, then the end-result would be greatly improved function. The rehabilitation of cases of rheumatoid arthritis that have had surgical interference is a great problem. The joints cannot be moved because of pain, and cases of capsulectomy sometimes end in bony ankylosis of the joint. With regard to osteoarthritis of the hip, may I quote "Osteoarthritis of the hip: a study of the nature and evolution of the disease" by Harrison, Schajowicz and Trueta (*J. Bone Jt. Surg.*, 35, B4, 624) "Osteoarthritis, as seen in the hip, is a disease which eventually embraces all the tissues of the joint but begins as a reaction of the juxta-chondral blood vessels to a degeneration of the articular cartilage; this reaction results in a hyperæmia of the bone. To our surprise we found that daily use preserves rather than 'wears out' articular cartilage; indeed, inadequate use is the commonest cause of cartilage degeneration and ensuing vascular invasion."

SUMMARY

With the advent of specific treatment for infection, recovery can be accelerated. The willingness and ability of a man to do his job can be increased by a balanced regime of rest and work, carried out in a Hospital or an organized Centre. It is this balance, designed for each individual patient which is so important in the stage of recovery.

Excessive activity of mind or body produces fatigue which militates against the production of full and efficient function in the minimum time.

Patients should be treated as people.

Traditional physiotherapy should be used as an aid and not become a "mental splint".

Muscle tone and bulk can be increased by stimulating normal communications between brain and limb, therefore active movements made directly and indirectly will produce efficient function. The more determined the patient the better the result.

CONCLUSION

A plea is made for the maintenance of the principle of therapeutic persistence in the production of a balanced regime of rest and activity. Physically and psychologically the patient will improve only when the ratio of rest and exercise is altered at the appropriate time. The country cannot afford numerous patients in hospitals for indefinite periods.

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Section of the History of Medicine

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[*October 7, 1953, contd.*]

Dr. Edward Wilson of the Antarctic

A Biographical Sketch, Followed by an Inquiry into the Nature of His Last Illness

By BERNARD J. FREEDMAN, M.R.C.P.
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EDWARD WILSON was one of the party of five that reached the South Pole with Captain Scott in 1912, and perished on the return journey. It was on the return journey that he sustained a painful leg condition, the account of which in his Journal leads me to believe that he suffered from a rare and interesting malady that sometimes follows over-exertion, namely ischæmic necrosis of the anterior crural muscles (also called the "anterior tibial syndrome"). The second part of this paper therefore deals with his penultimate illness rather than his last one which must have been the effects of inanition and exposure to cold. It is the rarity of the syndrome, coupled with the interest attaching to Dr. Wilson, that justifies an inquiry into the nature of his disorder.

I. BIOGRAPHICAL SKETCH

Edward Wilson was primarily a naturalist, with leanings towards zoology and especially ornithology. He was also a doctor and an artist. One receives the impression that to him medicine was mainly a part of his wider study of nature, and that painting and sketching, although a form of artistic expression, were principally a means of placing on record such natural phenomena as were noteworthy. Even so, in his drawing and painting he produced works of real artistic merit, and in his medical work he found a means of expressing his deep devotion to humanity.

He was born in 1872, the son of Dr. E. T. Wilson of Cheltenham. In childhood he early evinced an interest in nature study, and especially in bird life, an interest which was fostered by his father's practice of sending him on long country walks with instructions to make a record of everything noteworthy that he saw. At 14 he entered Cheltenham College as a day pupil, while residing at his mother's farm outside the town. At home, therefore, he had ample opportunities, denied to the boarders and town-dwelling pupils, of pursuing his nature studies. At 16, influenced by Darwin's notes on the voyage of the *Beagle*, he began to keep a journal, a practice which he maintained for the rest of his life.

He entered Caius College, Cambridge, on an Exhibition, where his neat lecture notes, so clearly illustrated, were in great demand by fellow-students. He did well at athletics and won his rowing colours and the University prize for diving. He entered St. George's Hospital in 1895, when he was 2 . Here his talent for draughtsmanship led to frequent requests from the consulting staff for drawings of specimens, and he illustrated the book on *Diseases of the Liver* by Dr. Rolleston (later Sir Humphry). However, long hours at study, slum work, taking children's religious services, and a life of self-imposed frugality ("Lodgings at 8s. a week and quite comfortable" he wrote to

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his father) led to a deterioration in his health. Rolleston diagnosed pulmonary tuberculosis. First, he took a holiday with friends in Norway, where he often stayed up until the early hours of the morning bird-watching, sketching, and collecting specimens in the northern twilight. He then spent eight months at Davos, where he found the atmosphere morbid and depressing, and his youthful exuberance led him to overdo grossly his allowances of exercise. He went for walks, many miles in length, and undertook steep, sometimes hazardous, climbs, all apparently without ill-effect. In spite of eighteen months lost through illness, he passed his M.B. examination two months after his return, in December 1899, and had his thesis on "Yellow atrophy of the liver" accepted the following year.

About this time (i.e. 1900, when he was 28) Capt. R. F. Scott was seeking a junior surgeon and zoologist for the forthcoming National Antarctic Expedition. Dr. Philip Sclater, President of the Zoological Society, and Sir Clements Markham, President of the Royal Geographical Society, recognizing Wilson's unusual combination of qualifications as naturalist, artist and doctor, recommended him to Scott, who was so favourably impressed that he took him on in spite of an adverse medical report. Meanwhile, on September 20, 1900, Wilson was appointed House Surgeon at Cheltenham Hospital, but unfortunately pricked his finger three weeks later at an autopsy. The resulting infection, complicated by axillary abscesses, necessitated his resignation from the post.

To fit himself for the Expedition he learnt taxidermy at the Zoo and studied Borchgrevink's collection at the Natural History Museum. Bernacchi (1938), who first met Wilson during these preparatory stages, describes him at this period as "inclined to be tall, very lean and frail looking, and

FIG. 1.—Dr. E. A. WILSON.   *Royal Geographical Society*

a little stooping. He had close-cut auburn hair, inclined to wave, blue eyes, was slightly freckled and had long slender hands. His voice was quiet, rather low-pitched, and he had a rather whimsical smile, sometimes inclined to be cynical. . . . He was a good listener, comforting to talk to and restful."

He set sail in the *Discovery* on August 6, 1901, just three weeks after his marriage. At South Trinidad Wilson secured a petrel unknown to the British Museum, and named after him *Aestrelata Wilsoni*. At Macquarie Island, 700 miles south-west of New Zealand, Wilson wrote, "I told the Pilot I would give him a bottle of liqueur if he could persuade the Skipper to allow us to land for collecting." In the three short hours available, he studied the King penguins and collected specimens

of nearly every species of bird on the island. The voyage went well, and it was not long before they landed on Cape Adare, which marks the north-western extremity of the Ross Sea. Here Wilson studied the Adélie penguin rookeries. As they sailed south alongside the western shore of the Ross Sea, he sketched and painted much of the mountain scenery. The hut, which was the Expedition's base on land, was erected on Ross Island, a volcanic island which juts out from the Great Ice Barrier at its western end. From here Wilson, with Scott and Shackleton, sledged 400 miles on the barrier surface to reach 82° 16′. All three came back with scurvy—Shackleton in desperate condition.

By the end of the second winter Wilson had completed about 200 coloured sketches of Antarctic scenery (several of which were reproduced in *The Voyage of the "Discovery"*), and a number of pictures of meteorological interest, such as lunar haloes, mock moons, fog bows and auroras. For reasons to be mentioned, he was especially interested in the Emperor penguin rookery, the only one then known, that had been discovered on the sea ice off Cape Crozier. The *Discovery* Expedition lasted in all three years and one month, and they arrived back in September 1904.

In 1905 he started a series of illustrations for a new edition of Bell's *British Mammals*, and for Yarrell's *British Birds*, on both of which he worked for five years. The former was published after he left on the *Terra Nova* Expedition and he never lived to see it in print. The latter unfortunately never saw light of day, as its publication was cancelled, though some of the illustrations were later reproduced in Hesketh Pritchard's *Sport in Wildest Britain* (1921). In 1905 a disastrous grouse disease swept the British Isles, and the Board of Agriculture appointed him field-naturalist to investigate it. This post entailed long hours on moorland, in committee room and laboratory. It kept him fully occupied and he performed about 2,000 post-mortems on the grouse in all. He eventually found that the disease was caused by a minute threadworm (*Trichostrongylus pergracilis*), which crawled up the fronds of heather and lay in the dew-drops on the ends of the young shoots on which the grouse fed. This parasite infested and ulcerated the bird's cæcum. Of the two quarto volumes which formed the report *The Grouse in Health and Disease*, Wilson wrote one-third, and the beautiful coloured plates were all by his hand. The report was published after he left on the 1910 *Terra Nova* Expedition, and this too he never lived to see in print.

In June 1910 the British Antarctic Expedition set sail in the *Terra Nova* and Wilson, now 38, went this time as Chief of Scientific Staff and Zoologist. "We want the scientific work", he wrote, "to make bagging the Pole merely an item in the results." Of the innumerable problems in all scientific fields that invited solution, one that particularly excited Wilson's interest was the early embryology of the Emperor penguin. He believed that the Emperor penguin was the most primitive example of this primitive bird, and he hoped that a study of its embryological development might throw light on certain evolutionary problems, such as the question of whether feathers have been evolved from reptilian scales, or whether they have an independent origin. Unfortunately, the Emperor penguin lays and incubates its egg during the coldest, darkest months of winter, and the only rookery then known was the one 67 miles away on the sea ice off Cape Crozier. This Winter Journey for penguin eggs, in which he was accompanied by Cherry-Garrard and Bowers, must be one of the most terrible and hazardous journeys ever voluntarily undertaken for a scientific purpose. Darkness was total, save for fitful gleams of moonlight, and the brief, faint twilight of midday. Cold was intense and often extreme, even for those parts (reaching 109·5°F. of frost on one occasion). A blizzard blew their tent away, and surfaces were so bad that, on some days, eight hours' sledging yielded only 3, 2 or even 1½ miles' progress. After barely escaping with their lives, they returned with 3 precious eggs. As Wilson modestly put it: "the weirdest bird-nesting expedition that has been or ever will be." The report of Professor Cossar Ewart, in which the embryological findings are evaluated, may be read in Cherry-Garrard's *Worst Journey in the World*.

Wilson as artist.—He displayed a natural facility for drawing from earliest childhood, and won the school prize four years in succession. An admirer of Turner, he was also influenced by Ruskin in the importance of precise representation. He was entirely self-taught. "I want to spend a year or two at least," he wrote, "in learning to draw, because the more I draw . . . the more hopeless I feel about ever being anything more than an amateur and a dabbler. What would I not give for a few years at a good art school." He illustrated C. E. Walker's book on fishing (*Old Flies in New Dresses*, 1897), in addition to the four publications already mentioned.

The 200 coloured sketches of Antarctic scenery and meteorological phenomena previously referred to were subsequently exhibited at the Bruton Galleries. Some of these were reproduced in the early editions of Scott's *Voyage of the "Discovery"* and the biography by George Seaver. He also made numerous drawings for the other specialists on the Expedition when these were needed to illustrate specimens, and these are to be seen in the *National Antarctic Expedition Report, Vol. II—Zoology.*

Scott wrote: "When it is fine and clear, at the end of our fatiguing days he will spend two or three hours seated at the door of the tent, sketching each detail of the splendid mountainous coast scene to the west. His sketches are most astonishingly accurate; I have tested his proportions by actual angular measurement and found them correct" (*Southern Journey*, 1902). He did his sketching

bare-handed. "There is nothing to fear", he wrote, "if you stop when you can no longer feel the pencil, then put on warm gloves." Impending snow blindness did not daunt his enthusiasm. " ou can only sketch when your eyes stop running—one eye at a time through a narrow slit in the sn w-goggles. . . . The softest B is as hard and gritty as an H."

His paintings and coloured sketches were done in watercolour.

Wilson as doctor.—His post-graduate clinical experience in England appears to have been lim ted to a locum-tenency at Cheltenham Hospital, followed by an appointment there as House Surg on in September 1900. He also gave attention to relatives when required, during the period he was engaged in investigating grouse disease.

On the *Discovery* expedition he went as junior surgeon and zoologist. On the *Terra Nova* expedi ion he was Chief of Scientific Staff, and his principal activities lay within the zoological and, to a smaller extent, the geological spheres. However, he freely gave his services medically, and all members spoke most highly of his devoted attention, often given in desperate circumstances, and with total disregard for his own comfort and safety.

Wilson's character.—Though it was not known to his companions at the time, we now know from his Journal and letters that he was motivated by deep religious sentiments which undoubtedly contributed to his great inner strength of character. He was a descendant of Quakers, and he hid these sentiments from formal outward expression. He was also influenced in his youth by Franciscan feelings of ascetic mysticism, and he believed in the perfecting power of pain.

"We who knew him", wrote Sir Charles Wright, the Expedition's physicist, "realized that though he kept himself as much in the background as possible, not a single man on the Expedition, from Capt. Scott down to myself, ever undertook any serious step without first asking Dr. Bill's advice. . . . The best influence and the finest character I for one will ever meet."

Scott wrote: "Words must always fail me when I talk of Bill Wilson. I believe he really is the finest character I ever met—the closer one gets to him, the more there is to admire. Every quality is so solid and dependable. . . . What ever the matter, one knows that Bill will be sound, shrewdly practical, intensely loyal and quite unselfish. . . . I hold him mainly responsible for the extraordinarily amicable relations which have existed among us."

And finally, Cherry-Garrard: "If you knew him you could not like him; you simply had to love him. Bill was of the salt of the earth. If I were asked what quality it was that made him so useful, and so lovable, I think I should answer that it was because he never for one moment thought of himself."

II. DID DR. E. A. WILSON SUFFER FROM ISCHÆMIC NECROSIS OF THE ANTERIOR CRURAL MUSCLES?

We will leave Wilson for a moment to discuss the anterior crural muscles, and the ischæmic necrosis which they may undergo after over-exertion. This syndrome is rare. So far only 15 cases have been reported, and I personally have seen one. In view of its rarity a *résumé* of its main features will be given. Relevant extracts from the diaries of members of the Polar Party will then be quoted, and their probable significance evaluated. The anterior crural muscles comprise the tibialis anterior, the extensor digitorum longus and the extensor hallucis longus. They occupy a rigid-walled osteo-fascial compartment bounded by the tibia, fibula, interosseous membrane and overlying fascia. In this compartment there is very little room for expansion. Consequently, anything which raises the pressure within it may obliterate the anterior tibial artery which supplies these muscles and which also lies within the same compartment. If this pressure is maintained for more than a few hours, ischæmic necrosis of the muscles ensues. Muscular œdema and possibly also minute intramuscular hæmorrhages would appear to be the means whereby over-exertion brings about a rise in pressure. This œdema would cause no more than the usual aching and stiffness after exercise in any muscle group less rigidly enclosed and less dependent for its blood supply on a single artery.

Marching or participation in games commonly precedes the onset. Soon after over-use of the leg muscles, the subject is seized with severe pain in the front of one leg, occasionally both. The anterior crural muscles become intensely painful, swollen, hard, acutely tender to pressure or stretching, and paralysed; a reddish-purple discoloration, bearing some resemblance to a bruise, appears in t e overlying skin, and there is loss of function in the anterior tibial nerve. During the succeeding seven to twenty-one days the pain, tenderness and induration in the affected muscle group subside. Althou h a variable amount of fibrosis takes place, movement may return if necrosis is incomplete or if musc e fibres regenerate. Incomplete forms of the syndrome occur. (Hughes, 1948; Carter *et al.*, 1949.

To return now to the Polar Party. They left the hut on Ross Island on November 1, 1911, a d reached the Pole eleven weeks later on January 17, after travelling 922 miles. The story of that ep c needs no re-telling. Physiologically it proved to be a tremendous drain on their vital resources. T e temperatures were much lower than had been anticipated, winds were adverse, and bad surface,

by slowing the party's rate of progress and increasing the expenditure of physical energy, simultaneously reduced the food ration and increased the calorific requirements.

Twelve days after starting on the return journey, and while still on the plateau, Wilson first mentions having trouble with his leg. For clinical details we must turn to the available accounts in the diaries of the Polar Party. First and foremost comes Wilson's own journal. A few gaps can be filled in from Scott's diary. Bowers kept a full diary but just at this period his time was monopolized by taking sights and keeping the meteorological log, and the part covering this period is consequently fragmentary and supplies no additional information. Seaman Evans and Oates kept no diaries. The MS. of Wilson's diary is, like Scott's, in the British Museum. It has not been published, but a number of extracts are quoted in Cherry-Garrard's *The Worst Journey in the World* (1922). It is of minor interest to note that Wilson made his entries in the 1910 issue of "Wellcome's Medical Diary and Visiting List". He made his day-to-day entries serially, without reference to the printed date.

Wilson Jan 28 Sun 15.7 m geog	We had fine day and a good march on very decent surface—a few isolated sastrugi [furrow in snow caused by wind], but otherwise nearly all surface wind marks like butterfly scales. . . . We are all on ski except Birdie [Bowers]. We are about 10,130 ft. above s.l. We are all pretty hungry. Could eat twice what we have, especially at lunch and breakfast,
Wilson Jan 29 Mon 19.5 m geog = 22 miles statute	We got in a very long march for 9 hours going over part good and part bad surface. There has been a lot of very glassy porcelain shell surface with raised foot prints and sledges tracks on it and enormous snow drifts and banks of hard crusted very deep cut sastrugi, awful for skiing over, but Scott and I were on ski the whole day—the other 3 on foot. I got a nasty bruise on the Tib. ant. which gave me great pain all the afternoon . . . Temp.—25 . . . Tonight about 87° 21'.
Wilson Jan 30 Tues 19.8 m geog	My left leg exceedingly painful all day so I gave Birdie my ski and hobbled alongside the sledge on foot. The whole of the Tibialis anticus is swollen and tight, and full of tenosynovitis, and the skin red and œdematous over the skin. But we made a very fine march with the help of a brisk breeze and a good going surface.

At Three Degree depot Wilson wrote:

Wilson Jan 31 Wed 13.5 m	Again walking by the sledge with swollen leg but not nearly so painful.. . . We have 1/10 extra pemmican in the hoosh now also. My leg pretty swollen again tonight.
Wilson Feb. 1 Thur 15.7 m	My leg much more comfortable, gave me no pain and I was able to pull all day holding on to the sledge. Still some œdema.
Scott Feb 2	Wilson's leg is better today, but might easily get bad again.
Scott Feb 3	Wilson's leg much better.
Wilson Feb 6 Tue [Feb 7	. . . Very cold march, many crevasses, I walking by the sledge on foot found a good many, the others all on ski. Upper Glacier depot].
Wilson Feb 14 Wed	We made a good day's march along the ridge of a very long pressure ridge. I was on foot and the rest all on ski.
Scott Feb 14	Wilson's leg still troubles him and he doesn't like to trust himself on ski.
Wilson Feb 15 Thur 13¾ m geog [Feb 17	I got on ski again first time since damaging my leg and was on them all day for 9 hours. It was a bit painful and swelled by the evening, and every night I put on a snow poultice. Lower Glacier depot; Seaman Evans died].
Wilson Feb 25 Sunday 11 m	Very good day's going on ski. Took on job of pace maker . . .
Scott March 8	Wilson's feet giving him trouble now, but this is mainly because he gives so much help to others. [This refers, however, to frostbite.]

Now, an analysis of the diaries yields the following information regarding Wilson's condition and activities. In the afternoon of a day's march of exceptional length (22 statute miles) over very difficult surface, the tibialis anterior muscle of his left leg became swollen, tight and exceedingly painful and the overlying skin was red and œdematous. The muscle was evidently under increased

tension and walking was extremely painful. In assessing the degree of pain and disability one can ot use ordinary criteria. The condition of the party was already giving rise to anxiety, and it was a c se of walk or die. Even Evans, though gravely ill, pulled on the day he died. Bearing this in mind, to h ve

British Museum

FIG. 2.—The page of Wilson's diary on which he first mentions his leg disability.
It is written in the 1910 issue of the Wellcome Medical Diary and Visiting List.

"hobbled alongside", as Wilson put it, without pulling during the first three days, and to ha e pulled on foot instead of ski for the next fourteen days, implies a greater degree of disability tha such activity would, under more normal circumstances, suggest. All who knew Wilson be

testimony to the fact that, when in pain, he was inclined to minimize his suffering; and we know from other instances that, when he sustained injuries, these received scant notice in his journal. Added force is thus lent to any comments he did make.

As regards the duration of symptoms, these were still present at the seventeenth day (Feb. 15) but apparently absent at the twenty-seventh day (Feb. 25). Perhaps twenty-one days might be taken as their approximate duration. The apparent complete recovery would appear to indicate a relatively mild attack. There is reasonably close correspondence between the data and the clinical picture the syndrome is known to present.

Appropriate contributory and precipitating factors are not lacking. On the day of onset (Jan. 29) an exceptionally long distance, 22 miles, was covered over bad surface, the average at that time being about 13 miles per day. The party were at an altitude of over 10,000 feet, and an atmospheric oxygen tension of two-thirds that at sea-level may have contributed to the ischæmia. They were all in deteriorating general condition from cold and under-nutrition. The food was inadequate in both quantity and quality, as judged by present-day standards.

What other conditions should be considered in the differential diagnosis? Wilson himself was clearly in some doubt. He first called it a bruise, but there is no history of his having received a blow. He later called it tenosynovitis, but the tendon sheaths are lower down, and he definitely placed the lesion in the tibialis anterior muscle. Since the syndrome was unknown at that time (and indeed is not widely known even to-day), it is not surprising that he used the terms "bruise" and "tenosynovitis" as these were the only conditions known to him that resembled his own.

Extensive rupture of a muscle can also cause bruising. But this gives immediate pain; moreover the group in question has a wide origin in length from bone, interosseous membrane and intramuscular septa, and it is indeed doubtful if it is ever the seat of gross rupture.

Thrombophlebitis is unusual over the tibialis anterior in the absence of varicose veins, and had this condition been present, Wilson would hardly have failed to diagnose it. I think it unlikely that incipient scurvy, with intramuscular hæmorrhage, was a factor. Had it been so, Wilson's condition would have progressively deteriorated; whereas in fact his leg condition improved. Wilson and Scott both had previous personal experience of scurvy (1902) and knew the symptoms, but it is not mentioned in their diaries; and Atkinson, who examined the bodies, found no trace. The diagnosis I suggested is of necessity hypothetical and retrospective since it is not possible to support it with morbid anatomical findings. It is an interesting conjecture that now after forty-two years the histological evidence still lies preserved, but virtually unattainable, beneath antarctic snows.

The onset, on the day of an exceptionally long march, of severe pain, swelling and raised tension in the tibialis anterior, the discoloration of the overlying skin, the disability of the first few days, and the persistence of swelling for about three weeks—all these details, gleaned from the diaries, correspond closely with the clinical picture which ischæmic necrosis of the anterior crural muscles is known to present.

There seems little reason to doubt that Dr. Edward Wilson of Scott's Last Expedition, suffered from a mild form of this condition. To Dr. Wilson goes, perhaps, the honour of writing the first clinical account.

SUMMARY

A brief account is given of the syndrome of ischæmic necrosis of the anterior crural muscles following exertion. Relevant extracts are quoted from the diaries of Dr. E. A. Wilson and Capt. R. F. Scott, of the 1910–13 British Antarctic Expedition, in support of the view that Wilson was himself a victim of this condition. These remarks are preceded by a biographical sketch.

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A Forgotten Psychiatrist—
Baron Ernst von Feuchtersleben, M.D., 1833

By CHARLES L. C. BURNS, M.R.C.S., L.R.C.P., D.P.M.

MY interest in the subject of this paper was aroused by mention of Dr. Feuchtersleben's name, and what he stood for, in a journal edited by Dr. G. Marañón of Madrid. He himself is one of those in our profession to whom we owe a share in the present revival of the Hippocratic tradition, or what may be described as humanistic medicine, for which Dr. Feuchtersleben stood in his day.

Baron Ernst von Feuchtersleben, M.D., was born at Vienna in 1806. His father was a nobleman holding office under the Austrian government, but his son chose a medical career, and graduated in 1833 with a thesis in Latin entitled *Doctrina de Indicationibus*. Shortly after, he wrote a commentary on *The First Book of Hippocrates on Diet*. A later book entitled *On the Dietetics of the Soul*, containing aphorisms and reflections of a philosophical and psychological nature, was a popular success; it was published in 1838 and translated into other tongues, including English.

In 1845 von Feuchtersleben was appointed Dean of the Faculty of Medicine at Vienna. His book *The Principles of Medical Psychology* (1845) was translated in 1847 for the Sydenham Society publications. "As a general rule", says the Editor, "the Society is unwilling to present its members with works which have not received the stamp of public approbation. Newly published books, like newly discovered ores, may be rich or poor; but to test their value, they require that the stream of time should flow over them, which fails not to carry away what is light and worthless, and leave the sterling metal alone behind. I ventured to suggest a departure from our rule in the present instance on account of the great interest which medical psychology at this time excites. . . ."

The Editor then begs his readers to give the book the whole of their deliberate attention, and not to be "discouraged or offended by the occasional occurrence of unusual words of clinical derivation".

The author tells us in his introduction that: "If we consider the science of medicine in general, and especially its present state, there is perhaps nothing so essential to its advancement as psychology, carefully adapted to medical purposes."

Replying to the charge that the study of medicine favours a disposition to materialism he says: "No one has more occasion than the physician to recognize the power of the mind and the perishable nature of matter; and if he does not attain to this recognition, the fault is not in the science but in himself, in not having thoroughly studied it, for here, we may say as Bacon did of philosophy, 'when superficially studied it excites doubt, when thoroughly explored it dispels it'."

We may say now that materialism did invade the realm of medicine, up to and including our own day, when, chiefly through the effect of depth psychology, the mind regained its place in medicine. But again there is a strong tendency to consider the distinction between mind and matter as merely one of linguistics, and to wish to rid ourselves of dualism resulting from the belief in what Professor Ryle has called "the Ghost in the Machine"; it will be of interest therefore to see how our Viennese physician treats of this problem.

True to the more philosophical approach to all problems which still characterized the period in which he wrote, and which to our detriment we have largely lost, our author starts by delineating and defining his subject: "Men have always recognized something which is termed spirit as distinct from body . . . the facts of consciousness, as well as those higher manifestations of the mind; its relation to the Good, the True and the Beautiful; the law of duty; the belief in something more exalted than that which is earthly, existed, and that in their fairest form, long before the thought was conceived of seeking the source of such wonderful effects in the organization of the human frame. Two worlds, the one intellectual, the other sensual, were equally given to us from the beginning, and all attempts to deduce them from one principle (except the Deity) have failed. This duality is the boundary line of philosophy; to have drawn it is the triumph of philosophy; to efface it, if that were possible, would be its destruction. Man therefore should be the link which connects the two worlds; and this is the problem, this is the enigma which can never be solved: for it is inconceivable how two essentially different principles each of which obeys different laws can be continued in one being."

He goes on to say: "But in man spirit is united, in a manner inconceivable by us, to matter. In this state of union, through which inert matter becomes an animated body, we call it mind. . . . Now it is this mind that constitutes the proper subject of our enquiries—spirit in its relation to corporeal life, organism in its relation to psychical life."

He makes constant reference to the Psyche and the Soma and their interdependence—anticipating in a remarkable way the modern views on this subject—but he simplifies the whole issue by claiming *mind* as the meeting place of body and spirit: the domain with which psychological medicine is concerned. Thus he avoided an excessive dualism or parallelism on the one hand, and, on the other, the over-simplification which our neo-materialists would fain bring about.

Following his preliminary philosophical observations, the author gives a very complete sketch of the history of mental disorders. He thinks that in the Golden Age of Greece there was "no occasion to notice the occurrence of these diseases". "But so soon as civilization degenerated into voluptuousness, they increased in number and intensity" and "... with the increase in refinement, the occurrence of nervous and mental disorders increased in a proportion which has been maintained to the present day". It is obvious that the Baron is in love with the Homeric age.

We cannot follow him through the various Greek philosophers and physicians but might mention the fact that Asclepiades believed in curing mental disorders by "exciting the energy of life through music, love, wine and employment"; also by "training in exercising the memory and fixing the attention".

Also that Thessalus believed in causing "a thorough commotion in the fundamental constitution of the organism".

The first writer on medical psychology is considered to be Celsus (born 30 B.C.) who considers three kinds of insanities: phrenitis which is a continual delirium; melancholy; and a third kind which lasts longer and is of two species according as the patient is deluded by merely false images, or by erroneous perception.

Of Galen he says: "This extraordinary man whose efforts were directed to restoring the declining art of medicine from the subtleties of the schools to the Hippocratic method, became himself the idol of a school which was more subtle than any other, and which departed for centuries from the Hippocratic system."

This ends the classical period and: "Henceforth the history of the world is covered with a vast nocturnal shadow, which was not dispelled by a rising dawn till towards the middle of the third period" (i.e. the late Middle Ages). "We see with regret", says our author, "that the entire art and science of enlightened antiquity vanished in the darkness of this night. But we must not judge rashly and unjustly the ways of Providence; for in this shadow, future births were hidden, and though we are unable to judge them, such periods of incubation are perhaps as important to history as the germinating process going on below the surface of the soil is to vegetable life. It was an age replete with fermentation; all nations were in commotion".

The Baron, like his contemporaries, seemed unaware of the flowering of philosophy with Thomas Aquinas (whose psychology of the Passions is much more "modern" that that which was to follow—up to Freud), but passes to what he calls the "modern age". He introduces us to the strange figure of Paracelsus, typical of the early Renaissance with its alchemy, astrology and crude science. So mentioning in passing the lonely figure of Stahl—defending vitalism against the prevalent materialism of his day—we come to the first psychiatrists: Pinel, Esquirol, and so to the main part of the book.

This is divided into four main sections: (1) Physiology. (2) Ætiology and Semeiology. (3) Pathology. (4) Therapeutics.

The chapter on Physiology starts again with a brief discussion on the relation between matter and spirit; insisting on their indivisible psychosomatic unity; but nevertheless also on the necessity of considering this unity as it manifests itself to us in terms of body and mind.

He makes no division then between physiology and psychology, for the chapter moves easily from one to the other.

Our knowledge of the external world is derived from the special senses mediated through spinal nerves. Apart from this we have *cœnesthesis* or "common feeling", organically represented by the ganglionic system of the sympathetic: the "nerves of semi-conduction" as they were termed by Reil. This system has three separate foci: the generative, the phrenic, and the solar plexus.

Whether the brain acted as a whole, or whether there were special areas e.g. for the *sensorium communis* and the cœnesthesias, appears to have been a matter of doubt; but the author assumes that at any rate the brain is the focus of represented images, and as such essential to mental action.

He mentions that at one time observations were conducted on the heads of decapitated criminals to discover whether sensation or even consciousness remained. It was said of one that when his name was pronounced, the closed eyes opened and turned towards the sound. Also that the face of Charlotte Corday after decapitation blushed at the behaviour of the executioner. Such observations the Baron dismisses with contempt.

With the consideration of the brain as the *sensorium* for images, we arrive at ideas and memory, and at the fact of consciousness itself. With regard to memory, the author is inclined to dismiss the idea of traces in the brain and postulates instead the notion of "vital tension" in the nervous structures, so that every nerve has, as it were, its own memory: truly an interesting point of view.

The idea of unconscious mind is adumbrated through the notion of "obscure ideas" or "sensations with dormant consciousness" which are held to be of great importance in medical psychology. The emotions are briefly mentioned and, we must note, there is no mention of instincts. These latter are apparently contained in the notion of *cænesthesis*.

The emotions are "heightened forms of feeling"; they are coloured by the antithesis "pleasure-displeasure".

The main divisions of mental operations are, as in later psychology: knowledge, feeling and desire. With the latter the distinction between "pleasure-unpleasure" becomes one between "love and hatred". (These distinctions have a familiar ring when we think of Freud.)

Here we must leave the "physiology" but might refer in passing to one of his remarks on dreams where he speaks of: "the delicate affinity of dreams with pathological states of the mind, where, too, as it were, the 'old Adam' appears, and is in every sense interesting to the physiological physician."

At several points the Baron mentions the importance of dreams, but he is as if afraid to commit himself to the view, which he merely adumbrates, that they may be indications of psychic states, and he rather lamely concludes with a list, which tabulates the morbid physical conditions corresponding to types of dreams.

It is in the chapter on *ætiology* and *symptomatology* that the Baron exhibits an attitude which is modern in the sense that he recognizes to the full the importance of what we now call the psychosomatic approach. Indeed his outlook and that of some of his contemporaries was ahead of his time; later obscured by the flood of discovery on the purely somatic side of medicine.

In discussing the possibilities with regard to this reciprocal psychosomatic action, he distinguishes between *degrees* of this relationship: first a general vague sensation from the state of body fluids, &c.; secondly, changes in the vegetative functions which will reach the mind only as "obscure ideas", and thirdly the direct effect of sensations which are fully conscious.

It is interesting to note a belief that the quality of transfused blood might have an effect on the disposition of the transfusee.

Although the results were uncertain, he says that wilder animals into which the blood of tamer ones was transfused showed themselves to be more timid, and vice versa.

The effect of the state of blood in depressing the spirits is mentioned and he says: "the spleen of the English is partly attributed to an endemic influence of this kind which corrupts the blood through the atmosphere".

A contemporary of his is also quoted, who connects the "endemic phlegma" in England with the endemic ossification of the membranes (i.e. the coating of arteries) which occurs in that country!

It is seldom that he makes statements which are to us incredible; but they tend to stand out as being quaint or amusing. It is noticeable, however, that authors of that time liked to point out acute or dramatic effects, such as sudden grief or joy causing actual death, or the body turning black with envy. He mentions that intense anxiety and grief will cause, among other things a disordered digestion, but does not recognize the role which we now attribute to chronic preoccupation and worry in digestive disorders.

The chapter on *pathology* opens curiously enough with a description of *somnambulism* leading to a consideration of *idio-magnetism* (which we call hypnosis). This to him is suspect and pathological, because, he says: "those who choose this subject of enquiry, are in general too much prepossessed in its favour to remain impartial. This difficulty is enhanced by the 'somnambulists' who, like spoiled girls, which they too often are, must have their own will, or they fall into convulsions."

He now arrives at the first systematic description of a "psychopathy", namely *hypochondriasis*. This is a much wider concept than the one we know, and is, in fact, the male form of that which in woman is called *hysteria*. He calls it an "inexhaustible disease" from its protean forms, but thinks that it is, in its essence, nothing but a *cænesthesis* heightened in all directions.

He is almost scornfully pitying of such a state:

"The hypochondriac presents a melancholy picture of the human mind under subjection to the body. The slave of his own caprices, now of the anxious fear of death, now of extravagant licence, he feels . . . all his maladies doubly and trebly—compelled as he is to see himself the laughing stock of his fellow-creatures, to whose weal or woe he is egotistically indifferent—and treated as a child or an idiot by his physician, who gives him crumbs of bread instead of pills" . . .

Hysteria differs from this according to the psycho-organic make-up of the female, so that "the stronger innervation becomes motor, and morbid movements (convulsions) prevail". The chief reflex action is directed less to the digestion than the sexual system. On the psychical side there is a more melancholy disposition, hence a constant tendency to weep.

(It would seem that in our time men are less, and women more, manly, since we do not find such a difference in hysteria as between the sexes.) He does, however, mention as one of the exciting causes, "the female education of our times, which combines everything that can heighten sensibility, weaken spontaneity, give a preponderance of the sexual sphere, and sanction the feelings and impulses that relate to it".

Leaving hysteria, and passing through disorders of the memory (on which subject he often quotes the Scottish physician Crichton), we come to disorders of fancy (or as we shall say: imagination), and thus to the *psychopathies* and *insanities*.

Of the *psychopathies*, insanity is merely the graver or more striking form. (Here again he is using the term psychopathy in its more accurate sense, whereas we mean something more like socio-pathy.)

To these he gives the general definition of *diseases of the personality* which "is the name we give to those compound conditions, in which the psycho-physical relation is diseased in various directions, so that the empirical personality of the individual appears thereby to be disturbed (or) disordered".

By the term "empirical personality" he excludes the abstract or "ethical" personality which may remain undisturbed but overlaid by the disorder; without this assumption, he says, "no cure of mental diseases by psychical means would be possible".

He then discusses the psychopathies under four main headings: (1) *Folly*. (2) *Fixed delusions.* (3) *Mania.* (4) *Idiocy.*

It is perhaps the most striking difference between our time and a century ago, that there was no clear distinction made between amentia and dementia: between mental deficiency and insanity. It is constantly stated in the book that all forms of insanity which are not cured are apt to end in idiocy, and this is evidently considered as the same in kind as congenital idiocy.

The author now surmises in a general way the prognosis of mental disorders. He says that the question—whether mental disorders in general are curable, either by nature or by art—may now be happily answered from experience, in the affirmative, but with respect to the proportions, criteria, &c. we cannot depend on the accuracy of statistical calculations.

He makes interesting observations regarding the influence of the patient's personality in prognosis, remarking, for example, that the psychosis is more difficult of cure the more it approaches to its corresponding temperament.

With regard to *therapeutics* the cures are divided into psychical and physical. The former range through the faculties of thought, feeling and will. Those measures which act through the senses are considered to be of the "corporeal" class, such as the effect of colour, sound, smoking (which is a method of "dissipating thoughts"), exercises for the memory, &c.

In talking of music he mentions with derision a suggestion made by Reil, who apparently went in for cures of the most fantastic and dramatic kind. This consisted in a "cats' harp", made by having a row of cats with their tails held down; on striking keys which had a sharp nail in them, the cats emitted a cacophony of howls.

He lays great stress on the value of employment which, he says, should not be pursued in the form of "treatment", but to the patient must seem to have an external object. He believes in rewards and punishments and definitely in restraint by physical means where necessary. (One finds in fact remnants of quite cruel treatment advocated with good intentions.)

He makes some observations on the approach of physician to patient. The physician, he says, "excites affection to himself when he bestows it with an honest and warm heart. It becomes a longing for him, provided he keep it within prudent bounds, which indeed is his duty as it is not to be supposed that he lives for one patient alone. With this limitation it is a mainspring in his treatment". He gives other rules of conduct: the physician should say very little to the insane, but he should behave towards them on the whole as if he had to do with people of sound mind. "The *tout ensemble*", he says, "must act upon the patient and press upon him like a surrounding atmosphere which he must recognize as a world in which he lives." With regard to lunatic asylums he has pertinent comments to offer. "The lunatic institution", he remarks, "as it might be, plays much the same part in the writing of the psychopathic physician, as Utopia, the Platonic republic, the Fortunate Islands, &c., do in those of the prose poets."

Again: "The situation should be isolated: that is so far from any large town, that neither the noise and bustle of the town can disturb the lunatics, nor that of the lunatics the large town. A patient who was asked by a visitor whether the loneliness of the residence was not irksome to him replied: 'I am more comfortable here in the little madhouse than there (pointing to the town), in the great one'."

"Harmony, the soul of architecture, should, even for the dead walls, attract and compose the mind of the patient."

He is not in favour of the suggestion made by the irresponsible Reil that these institutions should be known as "Boarding Establishments for Nervous Persons".

In a footnote he mentions the most ideal institution as being that of the village of the insane: the Colony of Gheel (a place ever since admired but little copied, except to some extent in America).

Finally with regard to administration he says: "the leading principles must be left to the physician, the details to the authorities, that is if psychiatrics are to be a branch of medicine and not of State ordinance."

With these wise words we may take leave of our friend Baron Ernst von Feuchtersleben, and reflect for a few moments on the work which I have done no more than to synopsize.

We have perhaps gained a perspective of what the science and art of psychiatry were a century ago.

He seemed to look back to earlier days with a certain relish in the dramatic and the unusual, even in a certain harshness of outlook; he was too much influenced by the prevailing tendency to find material causes, to be able to follow his own bent and take flight with the psyche.

One can see him on the verge, as it were, of this plunge, when he is dealing with mesmerism—or "idio-magnetism" as he called it—when talking of dreams; hinting at their possible psychological value, yet descending with a bump to the familiar physiological explanation.

His was too balanced a mind to follow all his intuitions; or his influence might have been greater. Like those of his predecessors, Stahl and Ideler, his voice was lost in the succeeding years which Dr. G. Zilboorg has described as the "era of systems" of which Kraepelin was the chief representative.

In many senses, however, Feuchtersleben was more "modern" in his approach than his successors, but terms like "old" or "new" are often merely conventional. Often our "new" ideas have been adumbrated in older times perhaps in mere hints, to emerge in a richer light after being overshadowed by later ideas and systems. Talking of the generations between Reil and Feuchtersleben, Dr. Zilboorg says: "These generations spoke the very language which the majority of the medical psychologists of the fifth decade of the twentieth century speak. Is the language, the thought, old or new?"

Feuchtersleben was certainly a precursor of the fuller knowledge of psychiatry which we now possess; in addition, he appeared to have had all the qualities of a great physician.

Section of Experimental Medicine and Therapeutics

President—G. A. H. BUTTLE, O.B.E., M.A., M.R.C.S., L.R.C.P.

[*December 8, 1953*]

WALTER ERNEST DIXON MEMORIAL LECTURE

[Number 7]

Clinical Pharmacology

By J. H. GADDUM, Sc.D., F.R.S.

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The Speaker started by paying tribute to Walter Ernest Dixon, in whose honour these lectures are given at intervals of three years (Gunn, 1932; Dale, 1935).

Pharmacological experiments on human beings started when the first medical man treated his first patient, for all good doctors are really doing experiments all the time. No two patients are quite alike and it is often necessary to find out by experiment what treatment suits each individual patient. The results of such experiments are stored up in the memory of the wise physician, but they do not always form a convincing, or reliable, guide for the rest of the world. When new remedies appear it becomes important to obtain objective evidence of their value in a form which is suitable for publication in a scientific journal. Pharmacologists have always been interested in this problem; some of the methods which they have used have been only distantly related to the problems of practical medicine, but in recent years similar methods have been applied to patients and I propose to discuss some of these clinical applications of pharmacology. I had already decided that the title of my lecture would be "Clinical Pharmacology" when I found that Dr. Harry Gold (1952) had used the same words to describe the same thing.

The first object of a therapeutic trial is to discover whether the patients who receive the treatment under investigation are cured more rapidly, more completely or more frequently, than they would have been without it. A physician can often form a reliable opinion on this question without being able to give the details of the evidence on which he relies, but in order to convince the rest of the world it is often necessary to make observations of some kind not only on the patients who receive the new treatment, but also on a control group who do not. Some physicians are content to compare what happens after the new treatment with accepted opinions about what happened before. Unfortunately these accepted opinions are not infallible. This kind of evidence is only convincing when the effects of the new treatment are striking and dramatic.

The observations which are made may be measurements of such things as temperature or weight or time in bed, or counts of such things as the number of patients cured or dead. It is, of course, important to choose the right thing to measure; an increase of weight may indicate a return of health or the onset of œdema. Many different things may be measured or counted, and it is customary to make many different kinds of observation in each case, since it is impossible to know in advance what changes the new treatment will make.

Control periods. The obvious way to assess a new treatment is to compare the results it gives with the results obtained before it was known. Since active immunization was introduced, diphtheria has killed fewer people than it did. There can be no reasonable doubt that these two things are cause and effect. Diphtheria is less fatal *because* immunization was introduced, but if there was no other evidence of the value of immunization, it would be unwise to argue that it must be a good thing just because its introduction has been followed by a fall in the number of deaths from diphtheria. During the same period scarlet fever also became less fatal; and it is not easy to say why this was, but it was presumably not due to the introduction of immunization to diphtheria. There is, of course, much other evidence showing that the introduction of immunization into a country or into an institution is soon followed by a fall in the mortality from diphtheria. Such evidence becomes convincing when the same experiment is repeated many times and found always to give the same result after about the same latent period, but it is always difficult to be quite certain that the *post hoc* means *propter hoc.* Changes in the incidence or severity of diseases in a hospital may be due to

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changes in the diet or changes in the nurses, which happened to coincide with the introduction of a new treatment. The value of the experiment depends on the skill and energy of the detective work undertaken to exclude the influence of such factors, but, in any case, it is not always possible to find the cause of changes in the virulence of diseases, which may be independent of treatment and yet occur at the same time.

In some chronic diseases it is possible to use each individual patient as his own control, by keeping him under observation for a control period before the treatment is applied. Many chronic diseases, however, have spontaneous remissions during which the patient is much better. In disseminated sclerosis, for example, or schizophrenia or tuberculosis the disease may disappear for months and the doctor may attribute this change to whatever treatment he was giving at the time. The study of remedies for such diseases demands especial care.

If the control period is long and the effect of the treatment is immediate, and if several control periods alternate with several periods of effective treatment, such experiments may be convincing, but generally speaking evidence based on control periods is much less satisfactory than evidence based on simultaneous controls. This is because it is never possible to be quite sure that the observed changes were due to the remedy and not to something else which happened at the same time.

Simultaneous controls. If a drug is given to some patients while others are kept as controls in the same places and at the same times, it is possible, with suitable precautions, to make sure that the drug is the only factor which could produce a significant difference between the two groups, so that if such a difference is observed, it must have been due to the drug.

James Lind (1753) carried out a well-designed experiment with simultaneous controls over 200 years ago. I will quote his own words, abbreviated:

"On the 20th of May, 1747, I took twelve patients in the scurvy . . . Their cases were as similar as I could have them . . . They lay together in one place and had one diet common to all. Two of these were ordered each a quart of cyder a day. Two others took twenty-five drops of elixir of vitriol three times a day upon an empty stomach. Two others took two spoonfuls of vinegar three times a day, upon an empty stomach. Two of the worst patients were put upon a course of sea-water. Of this they drank half a pint every day. Two others had each two oranges and one lemon given them every day. The two remaining patients took an electuary recommended by a hospital surgeon made of garlic, mustard, balsam of Peru and myrrh. The consequence was that the most sudden and visible good effects were perceived from the use of oranges and lemons; one of those who had taken them being at the end of six days fit for duty. The other was the best recovered of any in his condition and was appointed nurse to the rest of the sick."

This was not the first evidence that oranges and lemons were valuable in the treatment of scurvy, but it proved that they were more effective than various other forms of treatment recommended by different people at that time. The effect was rapid and easily observed, the experiment gave a clear-cut answer in a short time. When similar techniques are used to study the effect of slow remedies on diseases which are liable to disappear spontaneously, precautions are needed to avoid errors. These errors may be classified as errors of allocation and errors of assessment.

Errors of allocation occur when the patients are allocated to the two groups which will receive treatment and act as controls. The two groups should be as far as possible equal when the experiment starts. If the available patients are in two different hospitals, the simplest plan is to use one hospital for the treatment and the other for the controls. This helps to prevent the patients getting jealous of one another and diminishes the risk of mistakes, but it makes the results of the experiment practically worthless, since it is impossible to be certain that the result was not due to some unknown difference in the care of the patients in the two places. The most efficient experimental design involves the use of paired controls in which each treated patient is paired with a control patient in the same hospital, of the same sex, and similar as regards the severity of the disease, age and other known factors. When it is possible to select patients in this way the experiment is likely to give significant results with few observations, but it is often possible to get just as good results with slightly more labour on quite unselected patients.

The one absolutely essential requirement for a valid experiment, whether the controls are paired or not, is that the allocation to the two groups must be random. If there is any possibility of a *systematic* difference in the factors affecting the two groups apart from the treatment under study, it is impossible to be certain of the meaning of the result. If the patients are first chosen for the investigation, and then allocated to one group or the other by some random process, then there can be no systematic difference between the two groups and the significance of observed differences between them can be calculated from the differences between individual patients inside each group.

Patients are sometimes allocated alternately to the two groups, but this procedure may lead to error if the doctor who decides which patients shall be used in the experiment knows which group they will join (Gaddum, 1940). When the next case will be a control the doctor may be tempted to include a mild or doubtful case, or exclude a severe case and give it whatever treatment he himself believes to be most effective. Such decisions may be unconscious and yet spoil the experiment. A conscious attempt to avoid bias may produce a bias in the other direction.

Errors of assessment may occur when the results of the treatment are assessed by someone who may be too hopeful or too sceptical. Some doctors are unduly optimistic and others take an especial delight in disproving optimistic claims. One method of avoiding this type of error is to depend entirely on objective measurements of such things as temperature or weight. This is seldom very satisfactory, and it seems a pity to pay no attention at all to the doctor's opinion or to the patient's opinion. The only safe way to obtain unbiased opinions from either of them is to make them express their opinions without knowing whether the patient received an active drug or not. This is known in America as a double blind test (Greiner *et al.*, 1950). It generally involves giving the controls dummy treatment which cannot be distinguished from the real treatment. If the treatment is given in the form of tablets then the controls receive dummy tablets indistinguishable in appearance, taste and smell from the real tablets. These tablets are usually distinguished from one another only by code numbers and it is best to change the code from time to time so that the later results are not influenced by the rumours about the earlier results. Such tablets are sometimes called placebos, but it is better to call them dummies. According to the Shorter Oxford Dictionary the word placebo has been used since 1811 to mean a medicine given more to please than to benefit the patient. Dummy tablets are not particularly noted for the pleasure which they give to their recipients. One meaning of the word dummy is "a counterfeit object". This seems to me the right word to describe a form of treatment which is intended to have no effect and I follow those who use it. A placebo is something which is intended to act through a psychological mechanism. It is an aid to therapeutic suggestion, but the effect which it produces may be either psychological or physical. It may make the patient feel better without any obvious justification, or it may produce actual changes in such things as gastric secretion (DuBois, 1946; Wolf, 1950). Dummy tablets may, of course, act as placebos, but, if they do, they lose some of their value as dummy tablets. They have two real functions, one of which is to distinguish pharmacological effects from the effects of suggestion, and the other is to obtain an unbiased assessment of the result of the experiment.

In 1933 Evans and Hoyle carried out an experiment on the comparative value of drugs in the continuous treatment of angina pectoris. They used 90 patients to test 15 drugs, which were given at regular intervals without reference to attacks of angina. Most of these drugs had previously been recommended as effective and most of them received favourable reports from some of the patients. Dummy tablets were effective in about 40% of the cases; only 4 out of the 15 drugs produced better results than this and none of them did much better. Evans and Hoyle were thus driven to the conclusion that the good effects observed by others had been all, or nearly all, due to suggestion. They point out, however, that their results have no relation to the question of the value of certain drugs when used to abort or prevent individual attacks. This important paper probably owed something to Dixon's influence, since one of the authors was a close colleague of his. This technique with some improvements has been used by others in more recent years to study the effect of other drugs such as vitamin E (Travell *et al.*, 1949), khellin (Greiner *et al.*, 1950) and heparin (Rinzler *et al.*, 1953). All these authors agree that the effects of the drugs tested for the continuous treatment of angina pectoris were practically the same as the effects of dummy treatments.

Similar results were obtained in an extensive trial of an antihistamine in the treatment of the common cold. Extravagant claims were made a few years ago on behalf of the drug thonzylamine (or neo-hetramine), which was said to have beneficial effects in the prevention and treatment of colds. A committee of the Medical Research Council (1950) undertook an investigation involving 1,550 patients, half of whom received tablets containing the drug, while the other half received inert dummy tablets. The two kinds of tablet were indistinguishable from one another and the patients did not know which they were taking. The results obtained when the treatment started on the first day of the infection are typical of all the results (Table I). It was found that 13·4% of the treated patients considered themselves completely cured within twenty-four hours and 68·2% were definitely improved.

TABLE I.—TYPICAL RESULTS FROM AN EXPERIMENT ON THE COMMON COLD. TREATMENT
STARTS ON THE FIRST DAY. ASSESSMENT ON THE SECOND DAY

	Thonzylamine (Antihistamine)	Control (Inert tablets)
Number of patients	201	173
Cured	13·4%	13·9%
Cured or improved	68·2%	64·7%
Unpleasant effects attributed to the drug	20·9%	19·2%

(Medical Research Council Committee, 1950.)

It might have been thought that this was striking evidence in favour of the value of the drug, if it were not for the fact that inert tablets produced almost equally good results. It is interesting also that unpleasant side-effects attributed to the drug occurred just as frequently in both groups. It is evident that these effects were due to psychological causes.

These results illustrate the fact that those who keep no controls may think they have proved something when they have really proved nothing at all. This is sometimes called an error of the first kind. If the committee had kept no controls, they might have thought that their results proved the theory that the drug was effective. This would have been an error of the first kind. It might perhaps be thought that their actual results proved that the drug was not effective, but this would be an error of the second kind. The original theory is not proved, but it is also not disproved. It is still possible, though not likely, that someone else will plan some other type of experiment which will give a positive result. It is important in all such cases to avoid confusion between the verdicts of not proven and not guilty. The calculations which show that a result is not significant do not prove that it is not true.

Sometimes it is found that although the dummy treatment has some effect, the real treatment has more effect. The difference between these two effects is a measure of the pharmacological action of the drug which is being studied; it may be calculated as a percentage of its maximum possible value. For example, Glaser and Hervey (1951) estimated that out of 100 men 66 felt seasick on dummy tablets and 15 felt seasick on hyoscine. The difference between these figures is 51 and this is taken as the score made by the drug. Its maximum possible score by this method of calculation would be 66. Its effect is therefore calculated as $51 \times 100/66$ or 77%. This is the logic behind the formula known as Abbott's formula (Gaddum, 1953).

A more interesting and effective method of dealing with results of this kind is shown in an experiment by E. M. Jellinek (1946) on a headache remedy. The manufacturer wished to know the value of two of the drugs in this remedy known as b and c. Four kinds of tablet were made, indistinguishable in appearance and taste. The first contained b and c, the second c, the third b and the fourth contained nothing but lactose, which has no pharmacological action.

Each member of a group of 199 subjects who had frequent headaches, took a tablet whenever he had a headache and then decided whether the headache had been satisfactorily relieved or not. The patients were divided into four groups taking different tablets, and every two weeks the drugs were changed, so that after eight weeks all the patients had tried all the tablets. The percentage of headaches relieved by each kind of treatment was calculated and the results are shown in Table II. It will be seen

TABLE II.—PERCENTAGE OF HEADACHES CURED

Drug	199 patients	79 selected patients
b + c	84	88
c	80	67
b	80	77
Nil	52	0

(Jellinek, 1946.)

that lactose was effective in 52% of these headaches. The active drugs were more effective than lactose and there seemed at first to be no significant difference between the different active drugs. It was found, however, that the patients could be divided into two groups according to their response to lactose. One group contained all the patients whose headaches were ever cured by lactose. These headaches were presumably due, in part at least, to psychological causes. The other group contained 79 patients on whom lactose never had any action at all. These patients were presumably less susceptible to suggestive measures. The results obtained from these selected patients showed, to the satisfaction of the statisticians, that all three treatments were significantly different from one another; ingredient b was more effective than ingredient c, and both together were better still. These results illustrate the fact that in order to get significant results it is sometimes necessary to select the patients rather carefully.

Pulmonary Tuberculosis

Some of the principles which have been discussed are illustrated in the trials of remedies for pulmonary tuberculosis carried out in recent years under the guidance of committees appointed by the Medical Research Council (1948, 1953). The difficulty of assessing the effects of drugs on this disease is shown by the prolonged controversies which have raged over so many forms of treatment. Treatment with gold, for example, was introduced in 1924 and remained fashionable for about fifteen years without any real evidence of its value. This is well shown in Fig. 1, a graph prepared by D'Arcy Hart (1946) showing the number of papers on the treatment of tuberculosis with gold listed in the *Index Medicus* each year. Modern remedies have been assessed by properly designed experiments in a few months.

The first of these trials arranged by the Medical Research Council may be taken as typical. The patients were carefully selected and as uniform as possible. After they had been chosen as suitable they were allocated by a purely random process into groups receiving various treatments and groups acting as controls.

It was proposed at one time to give dummy injections to the control patients. If this had been done, it might have been possible to prevent the doctors from knowing which patients were controls. Clinical assessments of the progress of the patients would then certainly have been unbiased and could have been given full weight when the results of the trial were considered. The doctors did not like this

plan and it was obviously unfair to give intramuscular injections of inert solutions to some of these patients four times a day for four months; this proposal was therefore abandoned and the results were assessed in other ways.

The control patients never knew that they were control patients. They only knew that they had been admitted to hospital surprisingly quickly, and that they did not belong to the small group of patients who got special injections. All the patients spent six months in bed and received good general treatment. About half of them received 0·5 gramme of streptomycin by intramuscular injection every six hours for four months.

Measurements of temperature gave no clear information, although the average fall of temperature was slightly larger in the treated group. Measurements of weight also gave no information; the average weight increased in both groups. Streptomycin appeared to cause a fall in the erythrocyte sedimentation rate and in the number of bacteria in the sputum significantly greater than corresponding changes among the control patients.
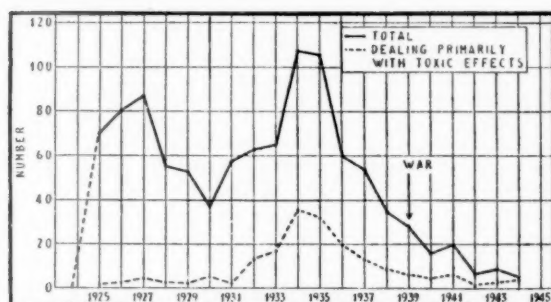

Fig. 1.—Graph showing the number of papers on gold treatment in tuberculosis listed in the *Index Medicus* during the years 1925 to 1944 (Hart, 1946).

More convincing results were obtained by examining radiographs of the chest (Table III). These were made before the experiment started and then at intervals of two months. Independent assessments

TABLE III.—STREPTOMYCIN TRIAL. PULMONARY TUBERCULOSIS

	Streptomycin	Controls
	% improved	
A Assessment of X-ray of chest		
0–2 months..	76	6
0–4 „	78	21
0–6 „	69	33
B Deaths in first six months		
Cases	55	52
Deaths	4	14
Per cent	7·3	26·9

(Medical Research Council Committee 1948.)

of these radiographs were made by 3 experts who did not know which patients they came from. They were asked to compare the original radiographs with those obtained two, four and six months later and to decide whether improvement had occurred or not. It was decided that improvement occurred in the first two months in 76% of the patients who received streptomycin and in only 6% of the controls. This is clear evidence of the effect of streptomycin in this disease. The result cannot have been biased because the assessors did not know what the effect of their decisions would be. The improvement was maintained for four months, after which many of the organisms had become resistant to the drug and the injections were stopped. The control patients also benefited from their treatment, but more slowly, and in smaller numbers.

It was also found in the same trial that 26·9% of the control patients died during the trial and only 7·3% of the patients treated with streptomycin (Table III). The statisticians tell us that this difference in the mortalities cannot have been due to chance, and our common sense tells us that it cannot have been due to bias in the doctors who decided that the patients were dead. It can only have been due to the streptomycin and yet it might have taken a long time to get such clear evidence if less care had been taken in the design of the trial.

During recent years this method has been much used. Different forms of treatment for tuberculosis have been compared with one another and their relative values assessed with unprecedented speed and certainty.

COMPARISON OF DIFFERENT DRUGS

Similar precautions must be taken when one drug is compared with another. In this case the question of the dose arises in a particularly acute form. Those who plan such comparisons are often content to decide on the appropriate dose for each drug in a more or less arbitrary way, and their critics then point out that the drugs which have had small effects might have had larger effects if the doses had been larger. It is therefore generally desirable to use more than one dose of each drug and to obtain estimates of the relative potencies of the various drugs. Much time has been spent in pharmacological laboratories on quantitative methods of comparing one drug with another by experiments on animals, but it is not sufficiently realized that similar methods are applicable to man. These methods may be classified as direct assays, assays depending on measured responses and assays depending on quantal (all or none) responses.

Direct Assays

In direct assays a measurement is made of the dose just necessary to produce a given effect. In Paxson's (1932) experiments (Fig. 2), amytal was given intravenously to women in labour in just sufficient quantities to relieve pain. The amount given to each of 55 women was recorded, and these results showed that the median effective dose (ED50) was 11 mg./per kg. The individual results were lognormally distributed with $\lambda = 0 \cdot 11$. It may be calculated that the standard error of this estimate of the median effective dose was less than 4%. It is thus clear that potencies can be accurately measured in this way.

In the same sort of way Hanzlik (1913) recorded the total amounts of salicylates given to a series of patients until toxic symptoms occurred (Fig. 3). The median effective dose was about 160 grains
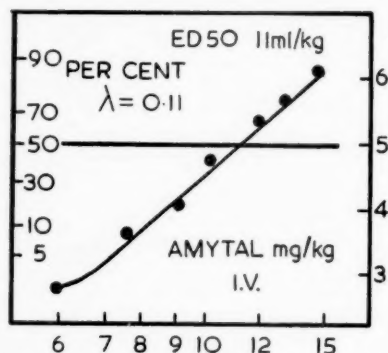
FIG. 2.—Effect of amobarbital on pain during labour. Horizontally—dose of amobarbital (amytal); log scale. Vertically—per cent of women protected from pain; probability scale (Paxson, 1932).
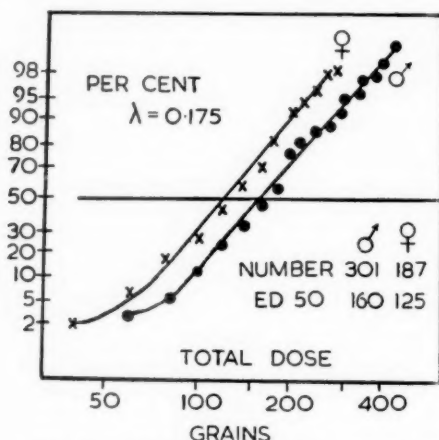
FIG. 3.—Total doses of salicylates for toxic effects. Horizontally—dose of sodium salicylate; log scale. Vertically—per cent of patients with toxic symptoms; probability scale. Women required less, presumably because their average weight was less (Hanzlik, 1913).

for men and 125 grains for women. The standard error of these estimates is only about 3%. The distributions were lognormal and the *mean* effective doses, as calculated by Hanzlik, were about 12% larger than these figures. This kind of discrepancy is what a mathematician would expect. Hanzlik used this method to compare the toxicity of allied drugs and found that aspirin and methylsalicylate were both just about as toxic as sodium salicylate or perhaps slightly more so, both for men and for women.

Direct assays were also used by Gold *et al.* (1942) for the assay of digitalis on human beings. The electrocardiograms of normal subjects were recorded before, and twenty-four hours after, a single dose of digitalis, which produced a depression of the T-wave. The experiment was repeated at intervals of one month and it was found that the effect increased when the dose increased, and that doses differing by only 22% could be distinguished from one another when assessed by the so-called blind technique in which the assessor does not know what effects his decisions will have. When each subject had been calibrated by giving him several doses of a standard preparation of digitalis, he received other preparations until a dose was found which had the same effect as one of the doses

of the standard preparation. The potency of the new preparation could then be calculated. Unna *et al.* (1950) used a similar method to compare tubocurarine with allied substances. They recorded the grip-strength at intervals after intravenous injections, and determined the dose of each drug just necessary to reduce the strength of their subjects to 5% of what it had been. They used 4 subjects once or twice a week for sixteen weeks and so made quite accurate estimates of the relative potencies of various drugs. The mean effective dose of tubocurarine was 107 µg./kg., of dimethyltubocurarine 41 µg. kg. and of decamethonium 20 µg./kg.

Measured Responses

Consider now assays depending on measured responses. Interesting results have been obtained by making continuous records on a drum of the human respiration, or the contractions of the human uterus, stomach, intestine, or gall bladder. Ergometrine was discovered as the result of the use of this kind of pharmacological technique. Such experiments depend upon apparatus which may seem a little complicated, but accurate results may be obtained and surprising conclusions reached with simple apparatus such as a ruler or a weighing machine. Professor W. A. Bain (1949, 1951) and Bain and his colleagues (1948, 1949) have carried out a series of investigations on antihistamines by this method. Standard doses of histamine were injected intradermally and the area of the wheal was measured. When antihistamines had been taken by the mouth the area of the wheal was smaller. The calculations depended on the percentage reduction of the wheal area, which was measured at various intervals after various doses of various drugs. When the effect, measured in this way, was plotted against time, the curve rose to a maximum in two to three hours and then fell fairly quickly after mepyramine and more slowly after the drugs with longer action. When the maximum effect was plotted against log dose each drug produced a straight line and all the lines were parallel so that the relative potencies could be calculated (Fig. 4). As a result of this work we have particularly reliable information about the relative activities of these drugs on man.
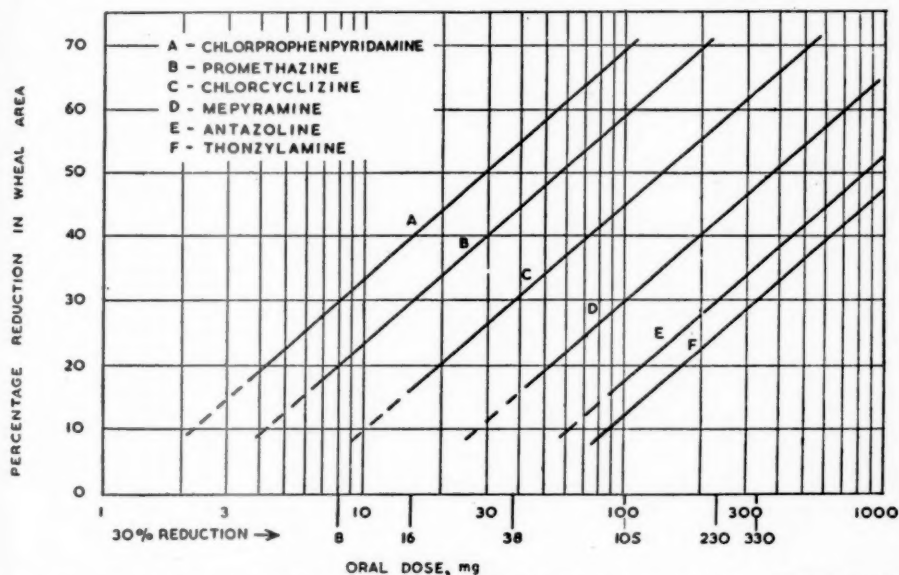
Fig. 4.—Comparison of antihistamines. Horizontally—dose of antihistamines; log scale. Vertically—effect (Bain, 1951).

A team of workers in Cornell University (Greiner *et al.*, 1951, 1953; Clarke *et al.*, 1950) has studied dose-effect curves for diuretics. The subjects of these experiments were outpatients with mild cardiac failure and œdema, who got some benefit from the drugs, but suffered no real hardship when the doses were reduced. The subjects were accurately weighed and given a dose of a mercurial diuretic. They were weighed again twenty-four hours later and the loss of weight was taken as a measure of the effect of the drug. A week later, when this effect was over, another dose was given and its effect recorded in the same way. Doses were randomized and the "double blind technique" was used, since psychological factors may affect not only the opinion of the patient on the effect of a drug, but also the amount of urine he passes.

It is surprising how much information was gained by this simple method. When the average effect was plotted against the dose the results lay on a curve, but when the effect was plotted against the logarithm of the dose the results could be fitted by a straight line (Figs. 5 and 6). When different drugs were used, parallel lines were obtained with either sex, but the male lines were steeper than the female lines. It is therefore difficult to compare the two sexes for sensitivity to these diuretics (Fig. 7). On the other hand, men were more reliable than women; it may be calculated that 10 men gave as
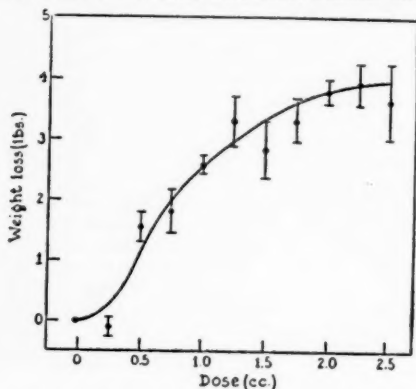
FIG. 5.—Dose effect curve for a diuretic. Horizontally—dose of meralluride (mercu-hydrin). Vertically—effect ± S.D. mean (Clarke et al., 1950).
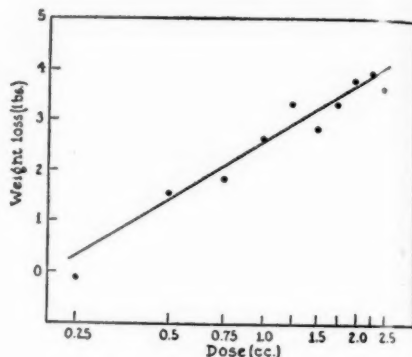
FIG. 6.—The same data as Fig. 5 plotted with a logarithmic scale of doses (Clarke et al., 1950).
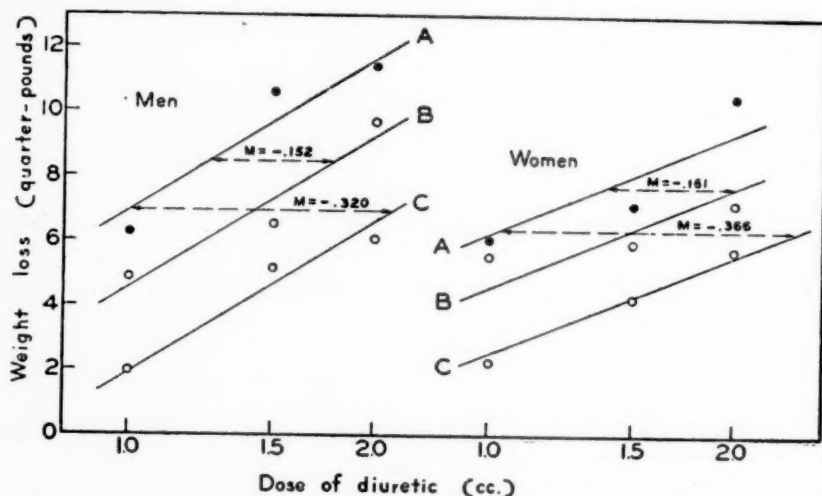
FIG. 7.—Horizontally—dose of diuretic; log scale. Vertically—effect. Effects of meralluride (A) and two other mercurial diuretics (B and C) on men and women (Greiner et al., 1951).

accurate information as 14 women. In view of all this it is perhaps comforting to know that the sexes were agreed about the relative potencies of the 3 different diuretics used in this investigation.

Many other points have been established by the same method. For example, it was found that when 8 grammes of ammonium chloride was given daily, the dose of a mercurial diuretic required to produce a given effect was only about 42% of the dose without ammonium chloride (Fig. 8). All these conclusions were confirmed by calculations which look as if they would gratify a professional statistician. It should perhaps be pointed out that these workers neglect the time factor, since they make all their observations at twenty-four hours after the dose. This simplification of their problem seems to be justified by the elegance of their conclusions (Greiner et al., 1953).

Quantal Effects

The third kind of method used by pharmacologists to assay drugs depends upon quantal effects. These effects are not measured but recorded as positive or absent and the number of positive effects is counted. This method was used in an experiment on analgesics by Keats *et al*. (1950). During the first thirty hours after operations, patients were given injections of drugs to relieve the pain. At intervals of 45 min. and 90 min. after each injection they were interviewed, and asked whether most of the pain had disappeared or not. If they said "yes" on both occasions, this was considered positive. Anything less than this counted as no effect at all. In order to test the method a constant dose of an unknown preparation was given to each patient and varying doses of morphine were also given to each patient. This was repeated about 50 times with each dose and the percentage of positive effects was calculated. The difference between this percentage for the unknown and the corresponding percentage for each dose of morphine on the same patients was calculated, and plotted against the dose of morphine. A line was fitted to the plotted points and the point on this line corresponding to zero corresponded to 10·8 mg. of morphine (Fig. 9). Actually the unknown dose was 10 mg. of
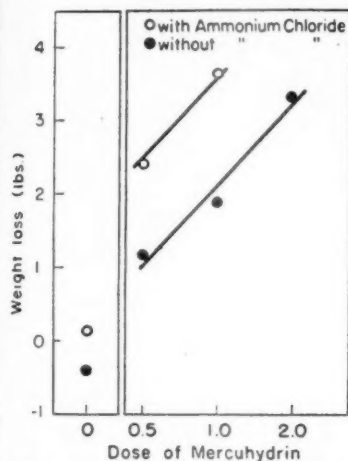

FIG. 8.—Horizontally — dose of diuretic, log scale. Vertically—effect. After ammonium chloride (8 grammes per day) the dose for a given effect is reduced to 42% (Greiner *et al*., 1953).
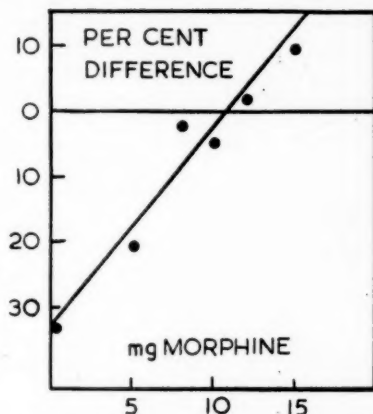
FIG. 9.—Comparison of analgesic potency of "unknown drug" (actually 10 mg. morphine) and of morphine. Horizontally—dose of morphine (mg.). Vertically—difference between per cent of responses to morphine and per cent of responses to unknown (Keats *et al*., 1950).

morphine, so that the error of the estimate obtained in this way was only 8%. This is not the conventional way of dealing with such data, but it gave a very satisfactory result. The experiment was perhaps rather laborious, but very simple to do. The potency of the unknown dose was accurately estimated under practical conditions when the drug was being used as it was intended to be used. Such experiments have more direct meaning than those in which artificial pain is applied to healthy volunteers. The general principles governing such experiments have been discussed by Beecher (1952).

Other workers on analgesics classify their pain as absent, slight, moderate or severe and probably get more accurate results in this way (Hewer *et al*., 1949; Macarthur and Alstead, 1953). The example quoted was chosen merely to illustrate the use of quantal effects. Similar methods have been used to study drugs that prevent vomiting. This is essentially a quantal phenomenon; it could not easily be measured, but can easily be counted (Chinn *et al*., 1953).

CONCLUSIONS

Many factors have contributed to the very rapid advance of therapeutics which has taken place in recent years. Fundamental work in physiology, pharmacology, biochemistry, pathology and bacteriology has increased our knowledge of nature and shown the way to new advances. The pharmaceutical industry has provided us with many new therapeutic tools, but new tools are not much use to those who cannot learn how to use them. Progress would have been less rapid if there had not been parallel advances in the technique of the clinical trial.

The examples I have given are from a large number of researches in this field. They were mostly carried out with very simple apparatus, or with no apparatus at all, and illustrate how much can be done with simple equipment, provided that certain general principles are recognized. In all these experiments simultaneous controls are preferable to control periods; errors of allocation must be

avoided and randomization achieved with certainty; errors of assessment can best be avoided by the use of the double blind technique, where neither the doctor nor the patient knows which patients receive the dummy treatment; when this is not possible the same object can sometimes be achieved by a compromise, such as that reached in the experiments on tuberculosis where the assessment was made by a second doctor who was not responsible for the care of the patients. If these precautions are taken, the subjective opinions of a group of patients can be interpreted with mathematical precision. All these things require careful planning and doctors who are not themselves statisticians should consult a professional statistician before they start their experiments.

In his Presidential Address to the Section of Physiology at the meeting of the British Association in 1929 Dixon tried to show that all precise knowledge in therapeutics is based upon controlled experiments on animals or man. The quarter of a century which has passed since that time has provided striking proof that he was right.

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Section of Otology

President—R. R. SIMPSON, F.R.C.S.Ed.

The Heritage of British Otology
PRESIDENT'S ADDRESS
By R. R. SIMPSON, F.R.C.S.Ed.

"As Practice is the last and chiefest part of Physick, so is
Observation the surest and most demonstrating part of
Practice."—*Dr. John Bird* (1657).

OUR heritage in British otology does not merely comprise a list of distinguished names, personalities, and traditions. It must also include some of the problems which have been left to us. Especially must it include something of the problems which have been left as an aftermath of the advent of the era of the sulphonamides and the antibiotics.

First, I must mention Sir William Macewen of Glasgow, the real Father of Modern Aseptic Surgery. It was he who maintained that he was a physician condemned to the practice of surgery. This philosophical approach to surgery was the culmination of a lifetime of research and experience. It explains, too, his advocacy of the reliance we should place on *vis medicatrix naturæ*—though some of that faith may have derived from his experience as a house-surgeon in Lister's wards in the days of "laudable pus". As students we realized that his serene composure was the product of both self-reliance and self-sufficiency. He was in himself his own complete research institution and his own craftsman. His operating table, for example, was made entirely of wood and to his own design. No modern gadget in stainless steel could do more to help a surgeon's needs than could Macewen's wooden table. His instruments were also made to his own design and had to comply with his high and severe standards.
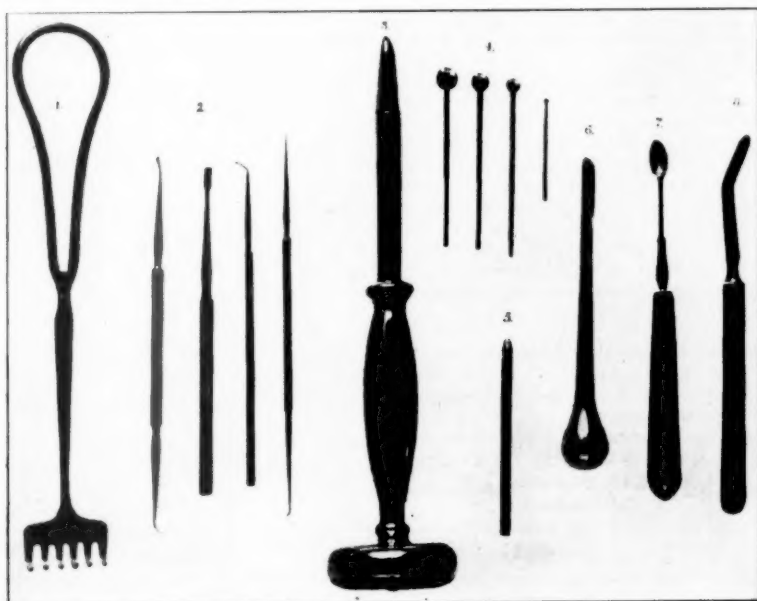

FIG. 1.—Sir William Macewen's instruments for mastoidectomy.

Fig. 1 looks like a tray of instruments set for the modern fenestration operation. It is, in fact, a photo-graph of the instruments Macewen used for the mastoid operation. It includes a retractor (1); a set of searcher and scoop, chisel, single and double ossicle hooks (2); a bone perforator—I believe Russian in origin (3); a set of rotatory burrs (4); a cerebral exploratory cannula (5); mastoid gouge (6); Volk-mann's spoon (7), and a periosteal elevator (8). The photograph was published originally in Macewen's book on "Pyogenic Infective Diseases of the Brain and Spinal Cord" (Glasgow, 1893). It is apt to be forgotten in this era of antibiotics that Macewen's results in the surgery of brain abscess had not only not been surpassed, they had never been approached until the advent of the sulphonamides and penicillin.

The late Dr. Albert Gray's fine collection of the fragile specimens of the actual membranous labyrinth of animals, prepared by himself, is unique and it is still to be seen in the Hunterian Museum at Glasgow University. Members will recall the beautiful and more permanent collection of casts of the cochlea and labyrinth prepared in the family tradition by his son, Dr. Oliver Gray, and shown here a year or so ago. Albert Gray's work on the histopathology of otosclerosis was outstanding, and his "Atlas of Otology" (Glasgow, 1924, 1933) is one of the classics of the specialty. His help and encouragement to younger specialists must be remembered and treasured by many members of this Section.

Albert Gray and J. S. Fraser both taught that in the more advanced stages of otosclerosis some degeneration of the cochlear branch of the VIII nerve occurred. It is possibly too early to ask the question, but I think those of us who are doing the fenestration operation must one day be prepared to say what does happen to the VIII nerve some years after the operation has been done.

J. S. Fraser will be remembered for his work on the histopathology of the labyrinth, which justly brought to his Edinburgh clinic visiting otologists from all parts of the world. His knowledge of congenital deaf-mutism was encyclopædic, as was also his insight into the breeding habits of the white bull-terriers which were the material for much of his work on the subject. His performance of the radical mastoid operation was a work of art and called for just as much concentration. His demands on his willing staff were equally exacting. I think I am right in saying that he shares with G. J. Jenkins the honour of being among the first to think of and to try the fenestration operation. That was in the days long before penicillin, and so their efforts were almost doomed to failure. The conception of the possibility was there, however, and they both deserve our remembrance.

I recall Fraser's long discussions on the types of labyrinthitis which could occur in chronic otitis media, the finer points in the diagnosis of each type of labyrinthitis, the indications for the Hinsberg operation and for the translabyrinthine drainage of West and Scott. There were, too, his discussions on Gradenigo's syndrome and petrositis. I doubt if anyone sees these operations done now, nor are they indicated to-day. It is even questionable, as Donald Watson pointed out in his Presidential Address (1948, *Proc. R. Soc. Med.*, **41**, 155) whether the labyrinth, in an early labyrinthitis associated with chronic otitis media, should be disturbed at all by having either the cold caloric test or the rotation test performed.

For Dan McKenzie I had a special regard: he was not only a mighty debater but also a persuasive teacher and was prepared to spend much time and trouble to help beginners. The great example of his method of exposition was, of course, his paper on cholesteatoma (McKenzie, 1931).

In 1939 my old chief and colleague, T. Ritchie Rodger, was President of this Section. His original paper on noise deafness was published in 1915. The hearing-tests he used were done with tuning-forks and monochord, for, of course, the audiometer had not even been thought of. Nevertheless his observations have stood the test of time. His Presidential Address was on deafness caused by syphilis. He reported 500 cases of syphilis of the ear, nose and throat seen in his clinic in the ten years, 1925–1934, an average of 50 a year for that period. By 1938, the yearly average of these cases had fallen to less than half that number, i.e. under 25. As I succeeded Ritchie Rodger in the same clinic, the follow-up can be considered comparable for the same area.

SYPHILITIC DEAFNESS

Since the war I have observed in the seven years 1946–1952, 71 cases of syphilis of the ear, nose and throat, i.e. an average of 10 a year—a most encouraging heritage when compared with the figures of twenty years ago. Of the 71 cases, all had positive Wassermann and Kahn reactions. In 30 cases the ear was involved.

The incidence as between the sexes was about equal, 16 males and 14 females. There were 7 congenital cases and 23 acquired. In 25 cases both ears were affected and in 5 only one ear was involved. The presenting symptoms were:

        (*a*) Deafness ..   ..   18 cases
        (*b*) Deafness, vertigo and tinnitus ..   ..   7 cases
        (*c*) Otorrhœa..   ..   ..   5 cases

Of the acquired cases it was possible to record audiograms in 37 ears. On looking over these audio-grams, it occurred to me that they showed features in common. Usually the audiogram shows a decline to the right with a tendency to a sharp loss of the frequencies above 2048. Another feature

which impressed me was that the lower tones showed a gradual decline up to the frequency 256 but at the frequency 512 the loss was not so marked; beyond that frequency the decline continued up to the sharp dip or absolute loss for the upper tones.   Six illustrative audiograms are shown.

AUDIOGRAMS I–VI
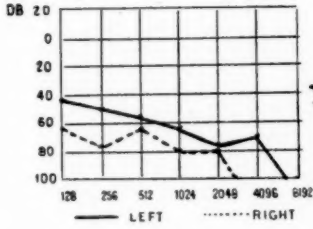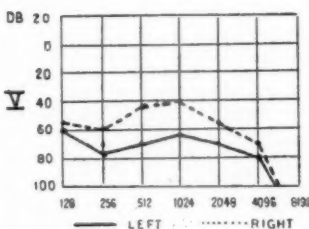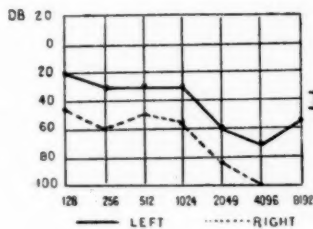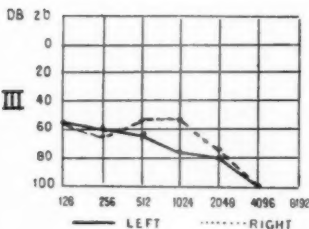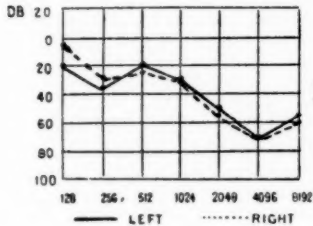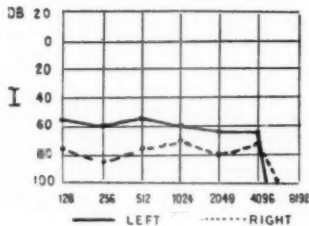
I.   Female, aged 37.   Deafness.
III.   Male, aged 69.   Deafness and C.S.O.M.
V.   Male, aged 72.   Deafness.

II.   Male, aged 73.   Deafness.
IV.   Male, aged 67.   Deafness.
VI.   Female, aged 57.   Deafness.

I took the average of all 37 audiograms at the various frequencies and plotted an **average** (Audiogram VII). This audiogram confirms the impressions I have mentioned.

AUDIOGRAM VII
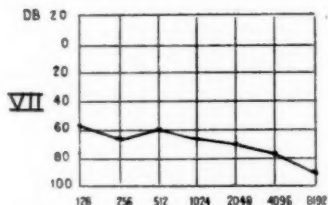
VII.   Average of 37 audiograms of syphilitic deafness—acquired.

The variation in the decline shown in this average audiogram may be of some significance. I would not say that such an audiogram is diagnostic; but I feel that if, in an unusual case of deafness, we come across an audiogram which shows something of that pattern, syphilis as a cause of the deafness should be suspected.

Perhaps I have said enough about the distinguished members of the Section of the past who have come within my own personal experience to illustrate the fact that we have inherited a record of very considerable achievement in British otology. I turn now from the personalities to the problems which may be regarded as part of the heritage of British otology. It will not be possible to refer to all of them but I shall discuss some of those which are of particular interest to me.

CHRONIC SUPPURATIVE OTITIS MEDIA

Despite penicillin and the sulphonamides, chronic otitis media is still met with every day by the otologist. It used to be regarded as a reproach to otology. Is this allegation still true? I have considered some of my figures of the condition in the pre-penicillin and the post-penicillin years. As a pilot scheme I have compared a short series of cases where the percentage and not the actual numbers was important—I wanted the impression rather than the statistics.

I have compared a series of 121 cases of chronic otitis media from the year 1933 with 89 of another series which I saw in 1946. In 1933, 56 of the 121 cases resisted all forms of conservative treatment and came to the radical mastoid operation, i.e. 46% of the series. In 1946, 24 of the 89 cases in the series resisted all forms of conservative treatment and came to operation, i.e. 27%. Of the 56 mastoid operations in the 1933 series, cholesteatoma was found in 25, i.e. in 44·6% of the mastoid operations for chronic otitis media. In 1946, of the 24 mastoid operations, cholesteatoma was found in 21, i.e. in 87%.

It is interesting—and salutary—to keep a constant check on one's accuracy in observation. In these two series of cases I wanted also to find out how often I had recorded in my Out-Patient Department notes whether I thought, on first examining the patient, cholesteatoma was present or not. This exercise does impose a very desirable and fairly strict discipline on one's handling of a new patient. Such a regimen is necessary in these days of unlimited aids to a diagnosis which could possibly be made on observation alone.

In 1933 I noted that I suspected cholesteatoma in 21 of the 121 cases. Of these 14 came to mastoid operation and in 11 of these cholesteatoma was present. That is, my observation was confirmed in 78·5% of the cases where confirmation was possible. In 1946, I noted my suspicion of cholesteatoma in 29 cases. Of these, 19 came to the mastoid operation and in 18 cholesteatoma was found. That is, the observation was confirmed where confirmation was possible in 94·7% of the cases.

Nager in 1925, in a large series of cases, found that 14·5% of ear, nose and throat out-patients were cases of chronic suppurative otitis media, and that of these one-third showed cholesteatoma. I wanted to compare that with the figures of the Edinburgh Royal Infirmary of about the same period and so I referred to a statistical survey in which I shared in 1927. To my surprise, there was no mention of cholesteatoma in the report. In a recent survey of 3,397 cases of chronic suppurative otitis media, Scott Stevenson (1949) found that only 106 required the radical mastoid operation, and of these only 37 had cholesteatoma, i.e. 35% of the radical mastoid operations; his figures for the incidence of cholesteatoma at operation are, therefore, the same as Nager's. In a still more recent series of cases, Hughes and McKenzie (1953) reported 28 cases of cholesteatoma in 41 mastoid operations for chronic otorrhœa, i.e. 68·3%. I felt certain that the figures of the pilot study I have mentioned represented fairly accurately my post-war experience. But to obtain the actual position I have reviewed 250 consecutive mastoid operations performed by me since 1946 for chronic suppurative otitis media which had resisted all kinds of conservative treatment, an average of just under 34 such operations per annum. At operation I found 218 mastoids showed cholesteatoma to be present, i.e. 87·2%. In theory that is what we should expect for, with the help of the antibiotics and the sulphonamides, we should be able to eliminate the majority of the straightforward infections of the middle ear and mastoid, provided cholesteatoma is not present.

As long ago as 1881, an American, Randall, asserted that "the cause of chronic or recurrent otorrhœa is cholesteatoma—a rule having few exceptions" (Randall, 1929). I am certain that no British otologist at that time, nor indeed even up to 1945, would have agreed with him. But when it is found that cholesteatoma is present in 9 out of every 10 mastoidectomies for chronic otitis, I confess that I am now bound to agree with that elderly American.

CHOLESTEATOMA

Since cholesteatoma figures so largely as a cause of resistant chronic otitis media and as the nature of the condition is still a mystery, some of the details in the series of 250 radical mastoids are of interest as a record of what I think is the present position. I shall deal with a few of the practical

points in diagnosis, in an attempt to assess their relative clinical value, and then I shall discuss my conception of the theory of the origin of cholesteatoma.

TABLE I

250 *Mastoid Operations for Chronic Suppurative Otitis Media*

Type of mastoid. *Acellular*	..	..	..	218 (87%)
Cholesteatoma found in		..	..	197
(i.e. in 90·4% of the acellular mastoids)				
Type of mastoid. *Cellular*	..	..	..	32
Cholesteatoma present		..	..	21
(i.e. in 65·6% of the cellular mastoids)				

In 116 cases the right mastoid was involved and in 134 the left.

While the advent of the antibiotics and the sulphonamides has relieved us of a great deal of mastoid surgery, it has left us one curious legacy. It is something of a paradox to realize that the mastoid surgery which we now do is technically more difficult. George Seed made some reference to this in 1950, when he drew attention to the small number of cortical mastoidectomies now done and the resulting loss of training opportunities for our registrars and house surgeons. The main type of mastoid operation now undertaken is for chronic otitis media. It is my experience since the war that of 250 mastoids opened because of chronic otitis media, 218 were acellular in type, i.e. 87%. When we remember that in the acellular mastoid the bone is densely sclerotic, the sinus is far forward, the dura is low, the antrum is deeply placed, the bone over the facial nerve is brittle and fractures easily, and that we cannot expect to find the mastoid with lots of elbow room for the beginner, we must surely feel a great sympathy for the trainee. But when we add to all these frightening thoughts the difficulty, for the beginner, of the endaural approach, then the prospect is truly alarming. There is little wonder that McGuckin emphasizes the absolute necessity for excellent lighting and adequate magnification in endaural surgery. Those of us who trained in the days of multiple emergency acute mastoids of the spacious type must surely conceive it our duty to see to it that the trainees of to-day have all the care and the time that we can find spent on our own personal supervision of their training.

Radiological findings.—The radiologists committed themselves to an opinion on the presence or absence of cholesteatoma in 203 instances. In 72 cases (35·5% of the total) they said there was radiological evidence of cholesteatoma and in 62 of these cases, cholesteatoma was found at operation, i.e. they were right in their positive findings in 86%. In 131 cases (64·5% of the total) where they found no radiological evidence of cholesteatoma, cholesteatoma was found at operation in 114, i.e. in 87% of their negative findings they were wrong.

Clinical findings.—Clinical examination showed the presence of cholesteatoma in 185 cases (74%) and in 174 of these, cholesteatoma was found at operation, i.e. the clinical observation was correct and was confirmed in 94%. Of the 65 cases where cholesteatoma was not noted clinically, 44 showed cholesteatoma at operation.

TABLE II.—SITE OF PERFORATION AND INCIDENCE OF CHOLESTEATOMA

1. *Attic perforation.* 85 cases (34% of total). Cholesteatoma present in 80.
    (94% of the attic perforations which came to operation)

2. *Polypi or granulations filling the meatus.* 61 cases (24·4% of total). Cholesteatoma was present in 45.
    (73·8% of this type which came to operation)

3. *Postero-superior quadrant.* 50 cases (20% of total). Cholesteatoma present in 49.
    (98% of this type which came to operation)

4. *Posterior half of membrane.* 36 cases (14·4% of total). Cholesteatoma present in 29.
    (80·55% of this type which came to operation)

5. *Attic and aditus erosions combined.* 18 cases (7·2% of total). Cholesteatoma present in 15.
    (83·3% of combined erosions which came to operation)

The percentage incidence of cholesteatoma given in Table II is, of course, in relation to the site of the perforation in those cases which came to the radical mastoid operation and not in relation to

the site of the perforation in chronic otitis media in general. It does probably bear some relation to the more general incidence; certainly the figures show clearly the high incidence of cholesteatoma in association with the postero-superior perforation (98%) and the attic perforation (94%).

Serum cholesterol.—Attempts have been made in the past to diagnose the presence of cholesteatoma by chemical tests on the aural discharge. There has been no recent report in the literature on these tests and so far as I am aware they have been abandoned. The biochemistry of cholesterol is as yet imperfectly understood, but it has been assumed that there is some relationship between the high serum cholesterol and the incidence of cholesteatoma. In this series of 250 mastoidectomies, the serum cholesterol was estimated in 81 cases.

TABLE III

1. In 65 cases the serum cholesterol was high (above 220 mg./100 ml.).
   In 60, cholesteatoma was found at operation (92%)

2. In 13 cases the serum cholesterol was normal (180–220 mg./100 ml.).
   In 12 cholesteatoma was found at operation (92%)

3. In 3 cases the serum cholesterol was low (below 180 mg./100 ml.).
   In all 3 cases cholesteatoma was found at operation.

I conclude, therefore, that while a high serum cholesterol may be of some value as confirmatory evidence of the presence of cholesteatoma, it is no certain indication of its presence; nor is it, in my experience, of any value at all as an indication either of the size or the extent of the cholesteatoma. My conclusions are at variance with those published by Bernovits in 1931.

Now I should like to discuss my own concept of the origin of cholesteatoma.

"BLACK" CHOLESTEATOMA

It is conceivable that the increased cholesterol content of the blood or serum is a pathogenic factor in the production of cholesteatoma. This brings me to the consideration of another aspect of cholesteatoma, and one which I have not heard discussed. It is, from its appearance at operation, what I have called "black" cholesteatoma. In the series of 250 mastoids, this condition was present in 6; in 1 patient it was bilateral. In all 6 cases the mastoids were cellular. In only 1 case was there
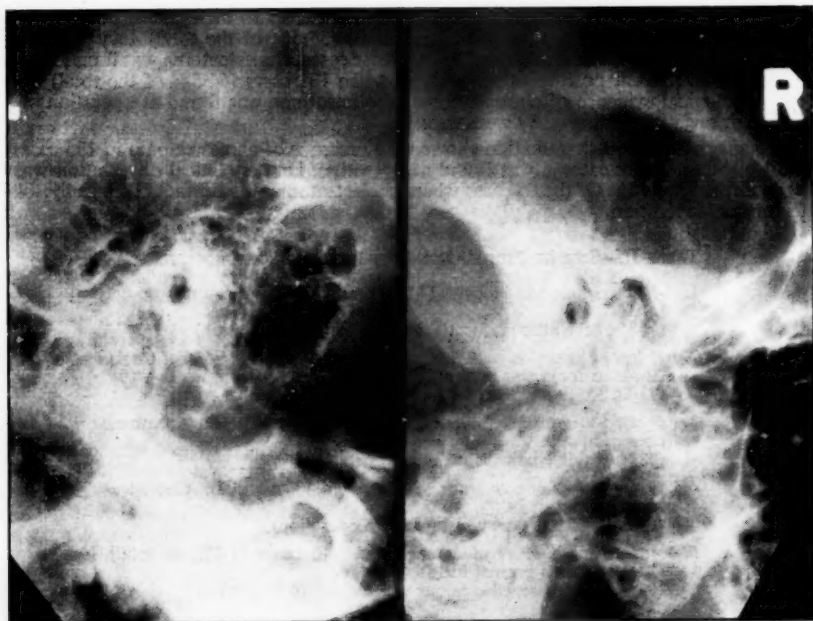
FIG. 2.—Extensive pneumatization of left mastoid. Right mastoid appears to be much less cellular, but at operation it was found to be very cellular.

any indication in the middle ear that such a condition might be present in the mastoid. In this case the middle ear was filled with what appeared to be—seen through the membrane—a blue-black fluid, the "blue" drum, which was thought to be an old hæmorrhage. Douglas Ranger in a recent paper on "idiopathic hæmotympanum" has discussed two similar cases. The details of my own case are:

Male, aged 27.—Recurring chronic otitis media (right) which began after swimming fourteen years ago. Present recurrence began with earache three days previously. There was a slight blood-stained discharge. Examination of the right ear showed what appeared to be the remains of a hæmorrhagic bulla over Shrapnell's membrane and a blood-stained effusion in the middle ear. The membrane was not bulging.

The condition was thought to be an influenzal type of acute otitis media and he was given a full course of penicillin by injection and sulphatriad by mouth. He was kept under observation but after a month the appearance of the membrane and the middle ear had not altered materially, except that a small pin-point perforation was seen in the posterior half of the membrane. The otorrhœa was always slight and there was never enough effusion in the middle ear to make me feel justified in either aspirating or incising.
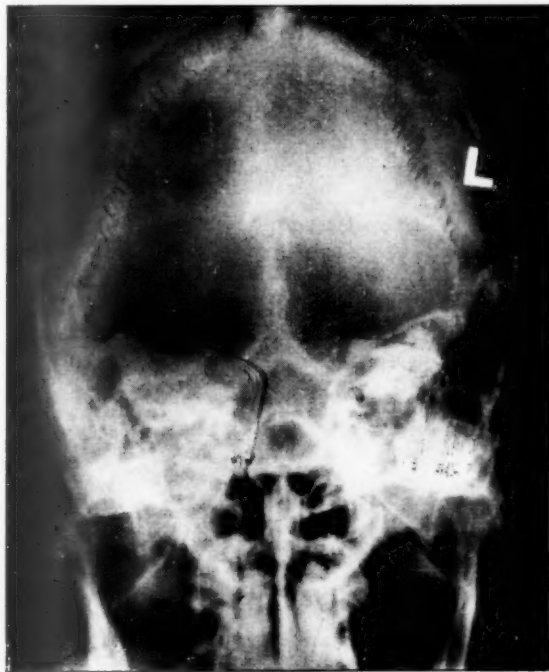
Fig. 3.—Deep extension of cells into petrous shown on left side. Similar extension of cells into petrous in right side found at operation.

At this time the radiologist's report on the mastoids was:

   Right mastoid: Air cells are hazy and sclerosed and there appears to have been complete destruction of the attic.

   Left mastoid: Air cells well pneumatized (*see* Figs. 2 and 3).

Four months after the onset, as there was no change in the condition of the middle ear or mastoid, he consented to operation.

At operation the cortex was found to be sclerotic but after removing this a very cellular mastoid structure was revealed. On this point I would make the same comment as Ranger, "it was a more cellular mastoid than appeared from the X-rays and there was no evidence of any infection". All the cells were filled with "black" cholesteatomatous material. There was a deep petrous extension of cells and they were filled with similar material. The attic was completely eroded and filled by the same material. On opening the middle ear black tarry fluid exuded. The ossicles were buried in this

o

material but showed no macroscopic change. Similar material was found in the eustachian tube end. Areas of the cell structure showed breaking of the intercellular trabeculæ but there was no eburnation of bone. The material was easily scooped out of the cells and, like the usual cholesteatoma, showed a pearly sheen where it had been attached to the bone. The blood in the mastoid cavity during the operation showed the characteristic oily appearance on the surface that one associates with cholesteatoma.
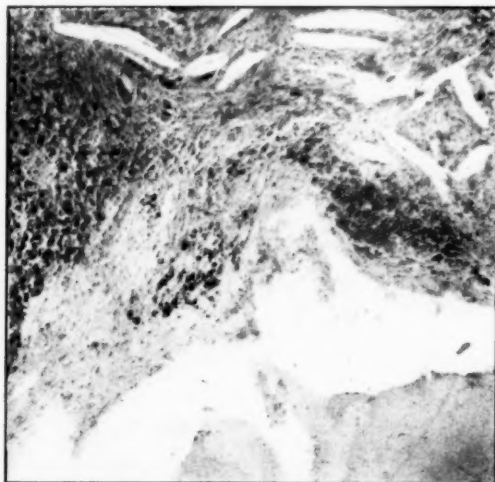
FIG. 4.—For description *see* text.

Pathological report (*No.* 1).—The specimen consists of a fragment of bone with some granulation tissue on its surface. The granulation tissue contains numerous cholesterol clefts and a fair amount of blood pigment which stains positively for iron. The granulation tissue is covered with cuboidal epithelium which does not show any tendency to squamous metaplasia (Fig. 4).

Pathological report (*No.* 2).—The section shows a fibroblastic granulation tissue in which there are numerous cholesterol clefts and scattered chronic inflammatory cells. Large collections of brown pigment, much of it intracellular within histiocytes, are also present. In the lower right-hand corner there is a fragment of bone showing osteoclasis (Fig. 4).

These reports correspond also to the findings in the two cases reported by Ranger.

There are two points in such a case which require some elucidation. The first is the possible source of the blood and the second is the source of the cholesterin crystals. It is possible that the correct explanation of both mysteries may help towards the explanation of the origin of cholesteatoma. Ranger found no satisfactory explanation for the origin of the blood in either of his cases and it is his opinion that the amount of blood was the result of repeated hæmorrhages. There was no obvious source in my case and I would agree that the amount present and the state of breaking down of the blood found suggests that more than one hæmorrhage had occurred, and over a long period. But how did these hæmorrhages arise? Going back to the history in my case, I noted that the patient sought advice because of earache occurring in an ear which had been discharging on and off for fourteen years. My first impression on examining the ear was that I was dealing with an influenzal type of acute otitis media with the remains of a hæmorrhagic bulla over Shrapnell's membrane and a blood-stained effusion in the middle ear. It is a common experience that *Hæmophilus influenzæ* causes mucosal hæmorrhages. They may recur during the acute phase and then cease. The initial hæmorrhage in my case may therefore have been due to this cause. But why did they keep on recurring over a period of weeks, and long after the acute influenzal phase had passed? Here I think the presence of the cholesterol crystals may come in. It is well known that the separation out of cholesterin crystals may occur in an enclosed hæmorrhage. If we imagine cholesterin crystals present, forming in a very confined space such as the attic and in the cells of a very cellular mastoid, we can conceive the effect of the tissue reaction, as shown in Figs. 4 and 5, on the cell mucosa and on the intercellular bone trabeculæ. The result we can well imagine would be small and recurring hæmorrhages from the mucosa and even from the intercellular trabeculæ, due to bone absorption. This happened to the cellular bone of the attic and to the cells of the mastoid in the case I have described.

As to the source of the cholesterin crystals, Ranger, in discussing this problem, concludes that they arise from the fluid filling the middle-ear cleft. This was shown to be altered blood, and it is established that cholesterin may crystallize out in this type of hæmorrhage. He also mentions a case of secretory otitis media on which a mastoid operation was done. Histological examination in this case showed cholesterin crystals in the mastoid but the amount was less than in the two cases of hæmotympanum. He makes the comment that this is in keeping with the fact that the cholesterol in serum is in a more soluble form than that in red corpuscles and is, therefore, less likely to crystallize out from the serum than from the blood.

But if the concentration of the cholesterol in the serum is greatly increased, it is conceivable that there would be a greater tendency for the cholesterol to crystallize out in circumstances such as I have postulated. In my own series of investigations, I find that in 45 cases where the serum cholesterol was considered to be unusually high, i.e. over 300 mg./100 ml., cholesteatoma was present in every case. There is the possibility, therefore, that in a patient who has a high serum cholesterol, deposits of cholesterin crystals could arise in any small serous effusion. Such effusions, as we know to our cost, can and do occur in the attic and the middle ear and the mastoid cells from various causes. It is thus possible that in such circumstances we have the beginnings of cholesteatoma. If this conception should prove correct, "cholesteatosis", as suggested by Gavin Young, would be a more accurate description, because the subsequent chain of events can be regarded as a tissue reaction to the presence of an endogenous foreign body—the cholesterin crystals. Such a tissue response would be a continuing one so long as the high level of the serum cholesterol persisted, because the serous effusion evoked by the tissue reaction would tend to produce still more cholesterin crystals. If, however, the serum cholesterol returned to normal, as we know it can do within a short period of time, the tissue reaction would be limited. An example would be those encysted attic cholesteatomas which have been in the past classified as "primary". Fig. 5 illustrates this point.
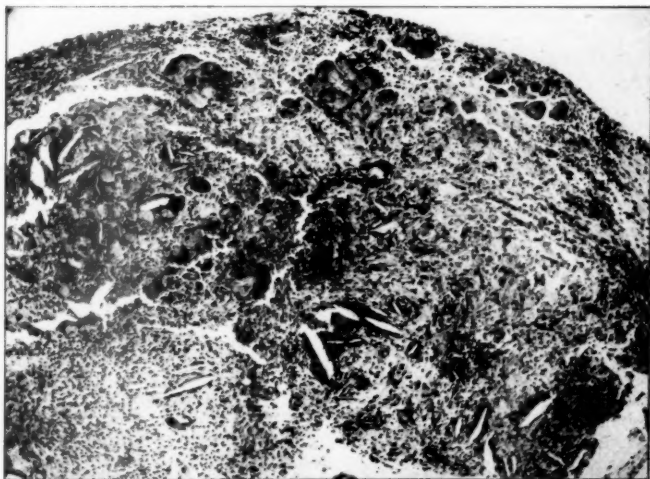
Fig. 5.—Section of small attic polypus showing cholesterin clefts with giant-cell activity very marked—the picture of the extrusion of a foreign body. (Section kindly lent by Mr. Guy Thompson.)

This conception has the advantage of being an explanation of the origin of all types of cholesteatoma, whether they are found in the attic, the antrum, the mastoid or even the petrous. It has the advantage, too, of dovetailing with all the points Dan McKenzie made about cholesteatoma. I shall consider only 3:

(1) In his conception of cholesteatoma being a primary condition, he stressed that "cholesteatoma may be found without any membrane whatever". If the conception that cholesteatoma begins as a tissue reaction to cholesterin crystals is accepted, then the question of a membrane being present is a late and a secondary matter.

(2) "The lining is sometimes found when examined microscopically to be devoid of epidermal cells." In the view I have expressed no epidermal cells need be present at all unless as a tissue response and then only as a tissue response of the lining cells. Here would arise the so-called meta-plasia, the changing of the simple cuboidal epithelium to the keratinized, resistant, epidermal cells.

(3) "It is noteworthy that the normal tissue, bone and connective tissue, beneath the cholesteatoma in the sections shown, betray no evidence of any inflammatory reaction"—the simple explanation being that in essence it is not an inflammatory reaction. Inflammatory reactions are found in many sections of cholesteatoma but they are due to secondary infections occurring after the initial cholesteatomatous change has started.

He maintained, too, that however large the cholesteatoma, it always presents a nidus, a point of origin, and that a closed cholesteatoma was devoid of fœtor. Thus he came very near to my conception of what happens but because of his preoccupation with the supposed function of the epidermal cells in the production of cholesteatoma, he failed to find a satisfactory explanation. "The epidermal cells", he said, "may, like osteoclasts, exercise a chemically solvent action on the bone upon which they are lying". But he thinks this conception is negatived by the fact that the living epidermal cells are not in immediate contact with bone, the fibroblastic layer lying between them. In my view, it is, of course, the cholesterin and not the epidermal cells which originate this action. Then he goes on to quote Kirchner on a point which I think adds some weight to my conception. Kirchner showed sections in which both epidermal cells and cholesteatomatous detritus were inside the Haversian canals of the bone in the neighbourhood where their action, whether mechanical—as Kirchner held, or biochemical—as I conceive it to be, would certainly lead to bone absorption.

The interesting practice of Sir James Dundas-Grant, of leaving the lining of the cholesteatomatous cavity instead of removing it, raises the question for those who maintain the epidermal metaplasia view, why were some of these cases of his so successful? If the epidermal cells were responsible for the cholesteatoma, they should have continued to produce it. On the other hand, if the epidermal cells are a direct response of the tissues to the presence of cholesterin—a protective response—then removal of the cholesterin should allow the epidermal cells to revert to their original function, and hence they will become true epidermis. This explains, too, the dry cavities seen on occasion when Nature herself has completed the radical mastoid operation.

It may be objected that I have not shown a high serum cholesterol to be present in every case of cholesteatoma. But I do not consider it necessary to do so. Little is known of the biochemistry of cholesterol. It varies within fairly wide limits in the normal person, but in some people it is persistently high. It should only be necessary to show that when the effusion first starts the serum cholesterol is high. But the case may only be seen months or years after cholesteatoma has been established, by which time the serum cholesterol may have returned to normal or even less. Neither pain nor deafness need be present in an attic effusion, and so it is unlikely that the patient will be seen in the earliest initial stage.

It is a line of investigation which will take a considerable time and much patience, but I feel it will be rewarding. If some such theory can eventually be established, then clearly, so far as we can judge at the moment, cholesteatoma cannot be prevented. The high incidence of cholesteatoma found in my series of mastoid operations for chronic otitis media—9 out of every 10 cases—would support the view that we are now able to deal conservatively with almost all cases of chronic otitis media which can be expected to respond to treatment, and that the failures in conservative treatment are due to the presence of cholesteatoma. Operation on these cases is inevitable in our present state of knowledge of the condition.

If it is conceded that in modern otology the failures in the treatment of chronic otitis media are due almost entirely to the presence of cholesteatoma, and if it is agreed that cholesteatoma is not only not preventable, but that when it does occur, operation is inevitable, then I think I have answered the question I posed at the beginning. We may claim that there is no longer any justification for the allegation that chronic otitis media is a reproach to otology. That is part of our heritage in which we can take some pride.

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Section of Psychiatry

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The Use of Vitamins in Psychiatric Practice [*Abridged*]

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THE paper opened with a review of the literature concerning the psychiatric uses of vitamins other than as dietary supplements. It was shown that the tendency was, in the acute psychoses, to exhibit one vitamin in high concentration assuming that dietary measures would suffice for the others, even though it was recognized that the administration of large amounts of one vitamin might precipitate signs of deficiency of others. This, together with the failure to appreciate the possibility of integration of action of vitamins, might account, not only for reports of clinical deterioration after the giving of large doses of one vitamin but for the conflicting evidence with regard to therapeutic effectiveness of any particular vitamin, as case records show that another had not infrequently been given in specific fashion immediately before the vitamin claimed as the "cure". Two other modes of employment of vitamins were described in the literature: (1) the giving of moderate amounts of mixed vitamins in certain organic states such as Korsakov's psychosis where the ætiological justification was doubted, even though the therapeutic value was more readily admitted; (2) the use of certain vitamins, notably nicotinic acid in "neurotic" or "neurasthenic" states (originating with the treatment of pellagrous subjects, the technique was extended and fell into disuse). (References to the literature have been omitted here; they will appear elsewhere, with a paper on Delirium Tremens.)

The personal contribution, which was then introduced had been commenced in 1944 in association with Dr. R. W. Armstrong of Oxford, in connexion with delirium tremens but had since then been modified and extended in application. Only the results in deliria, psychosis and coma due to drugs have been published (Gould, 1953). The initial premises were simple: delirium tremens was considered, as was common, to be a B_1 deficiency-disease-equivalent due to poor food intake. Remembering that spontaneously occurring vitamin deficiency was rarely single we gave "very large" amounts of several vitamins. Reference, at that time, to a small sample of the literature indicated the divergence of our approach from the single specific vitamin method, and the development of the technique has, since then, proceeded independently. The correlation of material deriving from clinical experience with physiological evidence, and rationale for the technique will be offered later.

The concepts guiding the further application of the method have been: (1) The clinical syndrome of the toxi-infective ("organic") psychosis in any degree of severity. (2) The toxi-organic psychosis regarded as an indication of metabolic disturbance of brain function due to toxins, drugs or intra-cellular derangement of metabolism. (3) Vitamins increasingly regarded as essential metabolic agents in brain respiration which is primarily carbohydrate respiration. Toxi-organic reactions found responsive to intensive mixed parenteral vitamin therapy may be subdivided into three groups: (1) pharmacologically determined disturbance of brain metabolism; (2) toxi-infective (somato-psychic) reactions accompanying or following acute infections; (3) temperamentally qualified reactions accompanying prolonged ill-health. (The number of cases is given in brackets.)

Group 1.—This group includes: (*a*) delirium tremens (10); (*b*) acute alcoholic psychoses (2); (*c*) post-operative confusional psychoses (8); (*d*) deliria due to drugs (4); (*e*) barbiturate coma (6); (*f*) collapse under continuous narcosis (2); (*g*) psychosis following continuous narcosis (4); (*h*) drug withdrawal syndromes (6); (*j*) continuous narcosis (which is a therapeutically contrived pharmacological disturbance of brain function). Excepting the last three named conditions (included with group 2) the others may be regarded conveniently as instances of acute insufficiency of vitamins for the purpose of brain respiration. These conditions (*a–f* inclusive) respond rapidly to intravenous administration, by drip, or directly into a vein, of glucose 3–10 grammes; vitamins C 1·5 grammes; B_1 1·0 gramme; nicotinamide 200–400 mg.; B_2 20 mg.; B_6 100–200 mg.; Pantothenic Acid 0–25 mg. This may be repeated in the absence of satisfactory response in four hours and followed by half the above amounts at four to eight hourly intervals as indicated clinically. The typical result is restoration to normality within twenty minutes to four hours. The desirability of these high concentrations is illustrated by 2 cases in which an initial satisfactory response was not maintained while treatment was interrupted for twenty-four to thirty-six hours, but recovery followed a further full dose. Where, as in a few cases, lung infection has also been present, more repeat doses seem required. The type of post-operative psychosis which responds to this treatment is that which develops soon after operation—usually within seventy-two hours. By contrast, 2 cases of confusional psychosis occurring

MAR.

seven and seventeen days after operation submitted to this technique failed to respond. One of these was a man submitted to gastrectomy for acute hæmatemesis. He had endured prolonged anoxia due to a relative hypotension of some 40–60 mm.Hg and an anæmia of 60% hæmoglobin for seventeen days in spite of transfusion of fifteen pints of blood. His delirium passed on into Korsakov's psychosis, whereas physical signs of vitamin lack responded to treatment.

Group 2 is regarded as illustrating subacute vitamin insufficiency in which, though brain respiration proceeds, integration and function are impaired. It is composed of two subgroups; the one pharmacologically determined includes the drug-withdrawal syndromes as traditionally understood, and an iatrogenic version, namely, the psychosis following continuous narcosis. I was led to treat the traditional withdrawal syndromes by this method on account of the restlessness and emotional upset—suggesting autonomic and other central disturbances during withdrawal, and the rapid quietening of psychotic behaviour found in the early cases of group 1. Heroin withdrawal syndromes (2 cases) have responded most favourably, morphine and pethidine less so, although considerable help was, in fact, obtained. A reduction of tension and emotional disturbance, and improvement in appetite and sleep were found. The doses found adequate are glucose 0–1 gramme, vitamins C 500 mg.; B_1 200–400 mg.; nicotinamide 100–300 mg.; B_2 10 mg.; B_6 100–200 mg.; Pantothenic Acid 0–25 mg. given intravenously twice or three times daily during withdrawal, later reducing the amounts. The psychosis following, on occasion, continuous narcosis, responds to this method, and, it would seem, may be averted by increasing the amounts of vitamins given as the barbiturates are withdrawn. The narcosis may become light if too large doses of vitamins are given during its course.

The other sub-group in group 2, includes the toxi-infective psychiatric syndromes associated with acute infections. Commonly the milder versions of these are accepted as part of the normal physical illness and convalescence, yet the virus infections in particular are well known for their toxic-depressive sequelæ. In these I have used glucose 0–1 gramme; vitamins C 300–500 mg.; B_1 50–200 mg.; nicotinamide 50–200 mg.; B_2 0–10 mg.; B_6 50–100 mg.; Pantothenic Acid 0–25 mg. given intravenously on up to ten occasions in most instances. Alternatively, daily injections of 2 c.c. of Betalin F.C. for up to twenty injections may be given. Although results appear more slowly, this is at times a more convenient method. I am indebted to Dr. B. S. Cooper who has investigated with me the toxi-infective cases and also the cases in group 3 for establishing the therapeutic value of this relatively small dose whose action in the aged may be dramatic (vitamin C 150 mg.; B_1 25 mg.; B_2 3 mg.; B_6 5 mg.; nicotinamide 50 mg.; Pantothenic Acid 2·5 mg.). The doses indicated serve to abolish the somato-psychic concomitants of these infections. Indeed, so marked is the change of clinical picture that, although the infection *per se* persists (and no claim is here made that it does not) the mental obfuscation resolves and the patient loses the sense of illness. Premature vigorous exercise is likely to precipitate a return of toxic symptoms, which, however, respond to further parenteral therapy. It is all the more necessary therefore, that an initial diagnosis be made carefully before the barrage of vitamins is laid on. The conditions which have responded include influenza and its sequelæ (25 cases); virus and bacterial pneumonia and their sequelæ (10 cases); sequelæ of varicella (2 cases); measles encephalitis (1 case); confusional insanity accompanying herpes (1 case). The response of the sequelæ of virus pneumonia is particularly gratifying and with intravenous medication profound improvement may be observed at once, complete recovery following in about seven to ten injections.

In my experience, if a depressive psychosis proper becomes established after virus illness, it does not respond to parenteral vitamins, although general well-being may be increased, and there are some indications that where parenteral vitamin therapy has been given for a time before E.C.T., memory impairment is reduced or absent, and tension does not arise in connexion with the treatment. With regard to dosage, the smaller amounts were used in the drug-withdrawal syndromes as treatment was expected to continue for some time. In the toxi-infective states, at first amounts were used comparable to those in group 1, but soon reduced, owing to the production of overdosage symptoms. The extension of this therapeutic technique from pharmacologically determined disorders of brain metabolism to the toxi-infective mental states was carried out on the grounds of the psychiatric similarities of the basic syndromes, in spite of the apparent diversity of ætiology. Toxi-organic syndromes are characterized by: (*a*) Interference with mental processes. (*b*) Exaggeration of temperamental traits. (*c*) Preponderance of emotionally charged material in awareness. These factors are characteristic of the psychological concomitants of influenza and many other acute infections, though in mild degree. Thus, if group 1 responded, the psychiatric concomitants of influenza, &c., should and did.

The case of measles encephalitis occurred in a boy of 10, with a long history of recurrent ill-health. During the resolution phase of measles he became somnolent, waking only for one hour in the forenoon and for another hour in the afternoon. He had been thus for seven days when an intravenous injection of vitamins restored normal interest and sleep and wakefulness. Two adults suffered from varicella and found that recovery of mental and physical well-being was slow, even though the infection had not been severe. They noticed exaggeration of psychogenic symptoms which had responded to conventional psychotherapy. Parenteral vitamins abolished the exacerbation of symptoms, and induced a significant increase in well-being. Similar experience has been obtained with several other patients who suffered from intercurrent virus infections whilst undergoing psychotherapy.

Group 3 may be described as temperamentally qualified psychiatric reactions to prolonged physical ill-health. The typical symptom picture is well known. Essential features are impairment of mental and physical resources, energy and well-being. Existing predispositions to psychological malaise are exaggerated. It is, if you will, the picture of "neurasthenia" and with this or some other diagnosis these patients are referred to the psychiatrist, having failed to respond to other measures. The physical disorders found in these patients include recurrent, recent, or co-existing respiratory infection; alimentary dysfunction (including conditions which necessitated gastrectomy); general infections; sequelæ of virus infections; multiple operations; chronic stress (85 cases). Both intravenous and intramuscular routes are suitable here. The dosage plan followed has been: (*a*) Intramuscular daily injections of Betalin F.C. 2 c.c. for twenty or more injections; (*b*) a progressively increasing daily intravenous dose, building up from vitamin C 500 mg.; B_1 50 mg.; nicotinamide 50 mg.; B_2 5 mg.; B_6 50 mg.; Pantothenic Acid nil; to vitamin C 1,000 mg., B_1 400 mg.; nicotinamide 400 mg., B_2 20 mg.; B_6 200 mg.; Pantothenic Acid 50 mg.; glucose has been given in amounts up to 1 gramme. The dose is then reduced, and if indicated a change to the oral route has been made. Parenteral treatment is far superior to oral therapy even when much greater amounts are given by mouth. Response to treatment again is gratifying with restoration of the normal psychiatric picture. By the intravenous route some patients may experience such an access of well-being that they become profligate for some hours and then find themselves exhausted. In some circumstances intramuscular injections are preferable even though a greater number are needed and results appear more slowly. One man ran seventy-five yards for a bus for the first time in four years the day after the sixth intramuscular injection. Another, a gross alcoholic who had undergone partial gastrectomy, became a good-humoured husband and father and realized a six-year-old intention to build a lean-to shed after working hours. A playwright with a history of much physical ill-health who had been unproductive for two years and unable to work satisfactorily for seven years was capable of writing six hundred finished words a day after eight intravenous injections. These conditions I regard as chronic vitamin insufficiency, and a number of these patients may possibly need maintenance for an indefinite time, either by additional oral intake or by spaced parenteral courses. Whether this be due to poor alimentary absorption I am unsure, but in some patients overdosage symptoms have been produced by oral dosage after parenteral therapy.

Some related miscellaneous observations may be noted here. Ascorbic acid, 200 mg. at night or on waking has been found valuable in combating the hangover effects of barbiturates, and for this purpose appears preferable to amphetamine. In the recovery phase after narcotherapy and electroplexy with anæsthesia, the effects of parenteral vitamins are in keeping with the results obtained in the pharmacologically determined disorders of group 1—the doses employed, however, being considerably smaller. Social protection against alcohol may be attained by those who desire it by the oral ingestion of vitamin C 200–600 mg., B_1 100–200 mg.; before and after the drinking bout and again the next morning. The larger doses would suffice to obviate the alcoholization (and also the socially sought disinhibition) associated with one and half bottles of wine and a couple of glasses of spirit.

Vitamin insufficiency.—The foregoing clinical observations imply an inadequacy of vitamin reserves in certain states. The term "Vitamin Insufficiency" was chosen to denote this concept which is different from vitamin deficiency as generally understood, the latter having its own history and connotations. *The manifestations of vitamin insufficiency* apparently occur in three associated modes: (1) Cutaneous lesions—were these to be vastly magnified they would begin to approach the normally accepted clinical syndromes of vitamin deficiency. (2*a*) Central nervous system—impairment and/or exaggeration of sleep, over-sensitivity to noise, light, &c., fatigability. (*b*) Autonomic symptoms. (*c*) Peripheral nerves—symptoms and signs of a very mild peripheral neuropathy. (3) Psychic manifestations, namely, exaggeration of temperamental traits and interference with the mental processes.

Not every patient exhibiting "Vitamin Insufficiency" betrays signs in all three modes, and such evidence is most common in the groups 2 and 3, regardless of the patient's general level of nutrition.

Generalizing: it appears possible that the more rapid the onset and the more severe the degree, of vitamin insufficiency, the more likely are psychiatric features to be overt. The slower the onset and the milder the insufficiency, the more probably will psychiatric features appear as coloration of attitudes of the patient, and the more overt will be the physical signs.

Overdosage with vitamins has generally been held, I believe, not to occur, except with vitamin D. Generally it has been assumed that ingested excess is excreted (Cowgill, 1943). Marked individual susceptibility to over-dosage appears to exist. As a mixture of vitamins has always been used, the observations on overdosage have been checked by varying any one component while keeping the others constant, but such observations should be taken as tentative.

Symptoms of overdosage.—B_1 *Acute* (more than 400 mg. I.V.): Acute mental alertness, without pressure of ideas, lasting a few hours. *Subacute* (after several days of injections): Lethargy, somnolence, mild ataxia, particularly for fine movements, heaviness in the limbs, diminution of gut tone—relief in forty-eight hours if vitamin B_1 be withheld. *Chronic* (dosage at any level above 5 mg. daily after greater dosage earlier): Thiamin is smelt in the newly washed skin, and in the excreta. Milder versions of the subacute symptoms develop, with nausea and lack of appetite though meals are eaten readily enough. Nausea responds to glucose by mouth. Relief occurs within 72 hours by omitting the vitamin.

Vitamin C: Overdosage occurs with 500 mg. daily or more, after giving much higher doses. Hot and cold sweaty feelings, ideational overactivity, insomnia, fullness in the head, headache, and increase of muscle tone and speed of reaction may occur. Relief occurs within 36 hours by omitting the vitamin.

Pantothenic Acid on occasion will produce abdominal spasm, irregularity of stools or rise of blood pressure. *Nicotinic acid* produces burning sensations, and on two occasions I have seen rigors follow its use. Therefore the amide is preferred, and has produced no clear-cut overdosage symptoms. *Pyridoxin and riboflavin*: in the amounts used, up to 400 mg. and 40 mg. respectively, overdosage symptoms have been absent. *Other effects*: Acute hypotension may occur with 300 mg. or more of B_1 but 1,000 mg. have been given intravenously with no alteration in blood pressure. Hypotension, e.g. 110/70, may be found in association with continued administration of B_1 and may be accompanied by subjective feelings of malaise. A few people become depressed on quite small doses of B_1. *Anaphylactic* shock has been described (Leitner, 1943; Reingold and Webb, 1946; Mills, 1941) in connexion with thiamin given alone intravenously at intervals. Others have attributed the sensitivity to the preservative (Jolliffe, 1941). So far anaphylaxis has not been met in this work. It is possible that there is less risk in the intravenous injection of mixed B vitamins than in B_1 alone, and vitamin C is considered by some to protect against anaphylaxis (Giroud *et al.*, 1936).

Body stores of vitamins.—According to Ferrebee *et al.* (1943) the thiamin content per gramme of various tissues is: heart 2–3 µg.; skeletal muscles 0·5 µg.; brain, liver and kidney 1 µg. Inadequate diet may halve these figures without inducing signs of vitamin deficiency in inactive (bed) patients. Taking 0·5 µg./gramme as an average figure a 70 kg. man has 35 mg. thiamin in his tissues, not accounting for thiamin combined as co-carboxylase. The daily requirement of thiamin is 1–2 mg. (say 1·5 mg.). The daily usage rate, therefore, works out at 5%. Heavy demands (as e.g. in pyrexia) may be put at three to four times the basic usage rate. In the absence of dietary intake, therefore, the body stores of thiamin would be reduced to 20–50% of normal in four days of heavy demand, which fits well with clinical observation. The position regarding ascorbic acid may be derived from Giroud's work (Giroud *et al.*, 1938*a*, *b*). Here arithmetic shows that in animals capable of synthesizing vitamin C, the muscle ascorbic acid content is approximately 1·5% of the adrenal ascorbic acid content. Applying this conversion factor to his figures of human adrenal ascorbic content, and calculating therefrom the total body ascorbic acid content of 70 kg. individuals at different ages, the results were: children 525 mg. (10%); adults 158 mg. (30%); old people 78 mg. (70%). One female of 84 years with vitamin C supplemented diet gave a corresponding figure of 840 mg. (6%). The daily usage rate (daily requirement taken as 50 mg./day, expressed as percentage of body stores) is given in brackets. Urbach *et al.* (1952) have correlated the blood level of ascorbic acid with toxi-infective stress and mood. These rough calculations are intended merely to draw attention to the poor state of bodily reserves in connexion, at any rate with thiamin and ascorbic acid. Deprivation of *nicotinic acid* rapidly leads to symptom production in certain conditions. The inference is that body reserves are relatively meagre.

Barbiturates and vitamins.—Barbiturates reduce the rate of oxygen uptake of brain tissue (Quastel, 1939). In the brain of a pigeon deprived of vitamin B_1 a reduction of O_2 uptake also occurs; this is corrected by thiamin and the R.Q. is raised to the normal level. In pellagrins there is a reduced O_2 uptake from the cerebral blood in the presence of an associated thiamin lack. It is possible therefore that the reduction of oxygen uptake with narcotics is due to the narcotics interfering with the same mechanisms as are involved in the vitamin lack. Clinically continuous narcosis occasionally precipitates signs of vitamin deficiency, often regarded as B_1 lack (Sargent and Slater, 1948), although signs of mixed B-group deficiency tend to be found. Occasionally, in the absence of excess of glucose, heavy barbiturate sedation may produce signs of B-group lack. This, together with the specific effect of mixed vitamins in acute barbiturate overdosage, suggests a direct "antagonistic" action. Thus the experimental and the clinical evidence are consistent with the idea that barbiturates exert their influence on brain respiration by inactivating enzyme systems. Thiamin, nicotinamide, and riboflavin occur in enzymes in the form of phosphorylated compounds (Barron, 1939). Conceivably barbiturates inactivate the enzyme systems by interference at this phosphorylation bond, or by adsorption on to the protein complex. Conceivably also the therapeutic effect of high concentrations of vitamins operates by "detaching" the barbiturate from the enzymes and "saturating" it, or by providing the raw materials for the synthesis of more enzymes. The former is in keeping with the evidence (Quastel, 1939) that the combination between narcotic and tissue is loose.

The discussion of delirium tremens from the clinical and physiological aspects is omitted. It will be published, together with the review of literature elsewhere. The summary follows: If this interpretation of delirium tremens be accepted (imperilling of carbohydrate respiration due to vitamin lack and forcing of alcohol as an alternative substratum), then it follows that in different cases, different factors may predominate. This reconciles the earlier conflicting evidence on the therapeutic value of glucose, fluid, thiamin and nicotinic acid and suggests that treatment should provide all relevant factors, with vitamins in amounts large enough to rectify the disturbed metabolic pattern of the brain.

Vitamins as catalysts and as metabolic agents.—Vitamins are commonly regarded as tissue catalysts, and as such remain unchanged by the metabolic reactions they facilitate. The small daily requirements of vitamins are held to support this view. Catalyst and enzyme are terms often used interchangeably.

Thus vitamin = catalyst = enzyme. Yet an alternative attitude is suggested by the evidence following:

Vitamins are exogenous constituents of intracellular enzymes (Elvehjem, 1943). They undergo synthesis (phosphorylation, e.g. in the cases of B_1, B_2, and nicotinamide) on absorption, before combination with a complex protein molecule whereupon enzymatic status is attained. They also undergo degradation and excretion in an altered form (e.g. uroflavine and nicotinuric acid or trigonelline). The daily requirement of vitamins is a significant proportion of the total body stores. Vitamin C is considered by some (Barron, 1939) to function in metabolic synthetic processes, and is present in amounts proportionate to the metabolic activity of the nervous tissue, whereas the B group serve respiration. In discussing evidence supporting the application of the law of mass action to the relationship of vitamins to enzymes and thus to tissue metabolism, the following points, among others, were made: (A) Experimental: (1) The concentrations of reactants determine the path of intracellular oxidations (Barron, 1939). (2) Excess of thiamin prevents the breakdown of co-carboxylase due to reduced atmospheric pressure (Govier, 1944). Recovery rates in vitamin-deprivation experiments depend directly on the size of the replacement dose. (3) Thiamin requirements depend directly on the total metabolism and upon temperature. (B) Clinical evidence is consistent with the above. (1) The large doses needed in acute nicotinic acid deficiency encephalopathy (Jolliffe, *et al.*, 1940; Sydenstricker *et al.*, 1938; Sydenstricker and Cleckley, 1941; Sydenstricker, 1943). (2) Clinical response rate in vitamin deficiency diseases depends upon dosage level. (3) The value of high blood levels of vitamins, presented earlier in the paper (Aring, 1941; Aring *et al.*, 1941).

Thus vitamins may be regarded as substances which, bearing a quantitative relationship to the total metabolism of the body, are themselves involved in a cycle of metabolism albeit one which does not dispose of large amounts of energy in its own right. Nevertheless, it is upon this cryptic metabolic cycle of the vitamins involved in carbohydrate respiration that the dynamically greater and metabolically more obvious cycle of carbohydrate metabolism is supported.

Rationale of technique.—If, indeed, one regards vitamins as metabolic agents, whose relation to cellular respiration mirrors in some measure the law of mass action, and remembers that the body stores of some of these substances are not only meagre, but are readily inactivated or rapidly reduced in certain circumstances, then the use of parenteral intensive mixed vitamin therapy in certain groups of clinical conditions (essentially toxi-organic and allied states) becomes reasonable on grounds other than clinical observation. Furthermore the value of the high blood concentrations of vitamins may be seen to reside in the possibility of influencing rapidly the equilibria between the various phases through which the vitamins are built up in the tissues to the enzymes in which they function within the cell, contributing to its metabolic integrity.

Vitamin insufficiency may be brought about by: (1) Decreased intake and/or absorption of vitamins. (2) Increased usage—i.e. increase of metabolism *whatever the cause*, physical or psychogenic. (3) Inactivation of the B vitamins enzyme systems due to narcotics, &c. (4) Intracellular derangement of metabolism by toxins or by virus invasion; in so far as this disturbance also responds to the administration of vitamins, it is possible that the vitamin components of the enzymes are again affected, or the response may involve the adrenal cortical system or both. (5) Two or more of these factors may operate together, as in alcoholism and in cases of chronic vitamin insufficiency following on ill-health. The diuretic effect of large doses of ascorbic acid, thiamin and nicotinamide do not, in the ordinary sense, account for the therapeutic effects, as fluids were never withheld and often encouraged because some of the cases were somewhat dehydrated. These agents may, however, effect a redistribution of intra- and extracellular fluids.

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PSYCHOTHERAPY IN PRISONS AND CORRECTIVE INSTITUTIONS [*Abridged*]

Dr. John C. Mackwood, London: Late Psychotherapist to H.M. Prison Commission, Wormwood Scrubs Prison.

The more serious the criminal act the more necessary is custodial control of the offender while psychotherapy is in progress, and until such time as it can be considered reasonably safe to relax this control. In prisons the idea of control is complicated by the intention of punishment, just as the idea of punishing an offender by sending him to prison confuses the two themes of the deterrent effect on others and any curative effect on himself. For many years the Prison Commissioners have realized the need for more scientific treatment as well as the desirability of lessening the daily deprivations and physical hardships, and treatment and rehabilitation methods under less severe but controlled environment have been increasingly extended since the war years by the provision of many new special and more "open" prisons.

Though some two-thirds or more of first-comers to prison do not again return, we never have been and never will be able to know whether this is due to their actual prison experience. Spontaneous remission of symptoms—and delinquency is a symptom of something amiss, whether pathological or psychopathological—is common in other psychiatric and organic disturbances of health. One might add that it is not fully recognized how many come to prison for behaviour that is common in the homes of a large section of the community.

External punishment and justice have fundamental roots in man's history, and it would be difficult to imagine how a moral conscience could form in a child without fears that accept punishment from outside as a help and relief to a primitive sense of guilt. The ordinary course of nurtural and educational development engenders an inner moral restriction which, in time, becomes effective in the absence of parental or representative authority. Psychotherapy makes use of the fear and anxiety in the criminal, where this is clinically present, to track back to the origins of his antisocial behaviour, and in various ways it can influence the start of a morale in many who had not previously shown indications of this power in themselves.

What makes active psychotherapy often difficult and frustrating in ordinary prisons is the fact that it requires special training discipline for a custodial staff to understand that successful psychotherapy, in those with unsolved neurotic conflicts that so largely contribute to their offences, acts through releasing instinctual energy that had been too much inhibited and was escaping sporadically as antisocial behaviour under the changing conditions and stress of modern life. This is particularly true of those offenders who can be categorized as psychoneurotic delinquency. These are usually good material in the early stages of their detection and need long treatment; they need to "work through" the uncovered aggressive urges in themselves, and this often involves behaviour that is disliked or punishable in prison. A staff that is not psychiatrically trained is uneven and does not understand this; and psychotherapy often requires an elasticity of control that cannot be expected in an ordinary prison where so many different types are housed under the same disciplinary regime. Moreover, for the purpose of research and the understanding of the genesis of crime, the trained psychotherapist cannot rest satisfied with good results from empirical or makeshift treatment—valuable and common as these often are; for they do not always hold when freedom restores the responsibility for his behaviour to the discharged offender. In fact, if one pauses to think, it is remarkable how law-abiding our prison population is in prison, by comparison with the results of American methods of shutting up large numbers behind secure barricades. Another factor we should not ignore is that it is usually easier to alter abnormal behaviour for the better than to alter really mature behaviour for the worse. Because of all these reasons the provision of a Special Centre for treatment has been a high priority for some years in the policy of the Prison Commissioners.

Evidence in favour of this reasoning has been forthcoming since the provision in Wormwood Scrubs in 1946 of a Special Ward of 10 beds, where offenders selected for treatment are housed apart from others. This is situated in the Hospital grounds and comes under the Senior Medical Officer for administration and discipline. It has the advantage of giving the offender the status of a sick person, protects him from unfavourable attention from his fellows not receiving this treatment, and

shields him from being involved in disciplinary incidents that are not of his own volition. But the greatest advantage has been the ability to start group treatment. This closed group is primarily a social one, and this is easily arranged by including a nucleus with definite neurotic manifestations. Its function is that of treatment, which arises spontaneously because this nucleus wants deliverance and endows the psychotherapist with powers to this end, as part of the transference phenomenon. The therapist can thus use the group in a specific manner by directing back into the group the power offered him in the transference, so that cross-transferences occur between the members and they discover new powers in themselves. A weekly group session provides very valuable pointers to progress and individual difficulties, and the ways that these are met or failure to do so; and these reactions are so openly expressed experiences that they can be taken up in the private interviews with the minimum of resistance from the patient.

Analytical psychotherapy has often been done within the framework of this group. One analyses as deep as is necessary to get out reliable memory and release of inhibitions and fixation points, and then it is necessary for the patient to work through the new material. It has been found that this ward provides an elasticity that gives improved results but there are limits to what can be done, limits that I feel sure could be removed in some special centre. The policy has been to send on these cases when sufficiently improved to selected modern or open-type prisons, where greater scope and understanding help them to acquire responsibility. They commonly go ahead there, but I have had a number of correspondents who have said that it was not until three, four or more years after discharge that they finally overcame their inner conflict, and accepted the giving up of some instinctual demands, and so felt safe and responsible for their behaviour. It makes one realize what risks such cases run, and how necessary it is for an organized psychiatric and social service that will support and take charge of them on their discharge.

Even more interesting is the effect of this social group treatment in starting moral (social) values in amoral offenders. The morale of this group sets its own limits of behaviour, limits that vary with the particular group and from time to time, and thus engenders a respect for the majority verdict. It has also a prognostic value, for anyone who rejects or is rejected by the group is not likely to respond to psychotherapy. The group has often overruled my initial assessment. It seems to have an intuitive capacity for differentiating between behaviour that is a malfunctioning of an inherently normal ego and behaviour that is due primarily to a malformed ego-structure, whether this is an intrinsic factor or environmentally acquired. I do not pretend to be able to explain exactly why a moral conscience, that is usually considered to require and to start within the family constellation, and is in abeyance, should begin in a social group of this kind. But it is so, and supports the observation that it is not difficult to alter abnormal behaviour.

This prison group brings out that the inherent factors of personality are of more importance than what a man comes to prison for. It was Freud who realized that any reliable idea of a norm must be approached with scientific methods of treating the abnormal: and in this way a serial development of the mind and ego emerged, and causes of malfunctioning could be isolated and dated. It is difficult for society and the law to avoid the opposite approach, for they feel themselves to be the custodians of what is valued as normal; but this must often entail considerable bias. Both views are necessary and need not be contradictory. This prison treatment group seems to have the qualities of a jury in arriving at a verdict on one of its members without being directed as to what is or what is not evidence of abnormality; and they are pretty accurate. It is a valuable pilot experiment that could be greatly extended at a special centre.

But the word group reminds us that the problem of crime is not the province of any one worker with his skilled discipline. All are complementary to each other. The value of psychotherapy, apart from its individual results, is in what it has done to isolate valid categories and to provide educators and sociologists with material to plan their researches. In the final analysis crime will prove to be a sociological problem even more than a social and individual one.

Dr. W. F. Roper, Principal Medical Officer, H.M. Prison, Wakefield:

Introduction.—The effect of imprisonment, as of all enforced residence in an institution, is to take the inmate back to childhood conditions. He again lies in the hands of those who have authority over him; his activities are again laid down for him; and he is no longer free to choose his own companions save amongst those with whom he is forced to consort. Nearly all of the difficulties noted by Dr. Mackwood arise out of this environmental regression in that they tend to force a behavioural regression upon the inmate.

On the face of it, this is a serious objection to all forms of institutional treatment, whether in prison or hospital. But it can be made an asset rather than a liability. The behavioural regression brings into the open the same kind of reactions which have built up the deviant character formation of the offender or which have involved him in neurotic conflict; it translates into the here and now the sort of reaction which otherwise has to be brought up again in memory and provides, therefore, an opportunity of readjustment. In short, imprisonment can re-create, in some measure, the former family and play-group situations and so give the opportunity of working over the actualities of the early formative period. What happens as a result of this reconstitution of old difficulties depends upon what is done to

adjust them; if nothing is done then they may become yet more fixed in the pattern of adult behaviour; if they are successfully adjusted then much benefit ensues. Here, as always, it is not the difficulty which matters; it is the way in which it is worked through; and for many years prisons, following the lead set by Borstal Institutions, have addressed themselves to the problem of enlightened man-management in an empirical way. The object has been to liberalize the regime to the greatest possible extent and to infuse it with wise paternalism and individual guidance. This is predominantly a lay achievement but where it has gone far enough it does provide a background against which some very useful medical and psychological work may be done; and it is reasonably successful in itself since over 80% of prisoners at a prison like Wakefield do not return to prison.

The Wakefield Regime.—Wakefield Prison deals with early offenders drawn from all parts of England and Wales and was the prototype upon which the many Training Prisons which have grown up since were modelled.

It was first opened as a Training Prison in 1923 and in 1947 a Psychiatric Unit was set up in order to treat prisoners who needed psychological treatment; some of these are sent specially for the purpose; others are found from within the existing population. There have been many difficulties of staffing which have made for an uneven development; at the moment there are two full-time medical officers, two part-time visiting psychotherapists, a psychologist and an assistant tester, and, when we can get one, a Psychiatric Social Worker.

All prisoners come from some other prison on transfer and may come from any part of the country. They are all screened as soon as possible after arrival so as to lay down a treatment plan for each, where necessary, as soon as possible. I will not go into the details of the screening other than to say that it includes group intelligence tests, such other tests as may be required, the taking of a life-history and a general review of their physical and mental condition. The result is to divide the whole intake of some 500 a year into three groups from the medical point of view. About two-thirds are left to the general training programme of the prison; the other third are marked, in addition, for periodical medical review and minor psychotherapy at the hands of the whole-time medical staff; and, from this third, certain cases are selected for submission to the psychotherapist with a view to treatment. They may, of course, be rejected, but this does not often occur; if they are, then adjustive treatment by the whole-time medical staff must suffice.

All cases treated by the psychotherapists are also kept under review by a medical officer through whom all requests for environmental adjustment must pass. This relieves the psychotherapist of all responsibility for environmental adjustment so that the prisoner stands to gain nothing from the treatment except the treatment; but, of course, any suggestions made by the psychotherapist are carefully considered.

The difficulties of environmental management are dealt with by the whole-time medical officers with the co-operation of the Governor and his staff. Adjustments are made when necessary but the general idea communicated to the prisoner is that the business of medical men is to make people fit to do what is asked of them rather than to cause them to be excused. Given the background of understanding and sympathy which has been gained from the initial interview and subsequent reviews it is not too difficult to establish this necessary idea.

In addition a good deal of minor psychotherapy is done by the medical officers; it is often surprisingly easy to bring a prisoner to see that he is engaged in fighting a battle long past and that the attitudes carried forward from an earlier phase of his development are the effective cause of his present difficulties. Once he has grasped this he has the opportunity of working out new relationships and this is an opportunity which he often takes.

The difficulties of psychotherapy in prison.—These fall under five main headings:

(1) Difficulties of selection and timing. (2) Difficulties of weaning and after-care. (3) Difficulties connected with relatives and domestic anxieties. (4) Difficulties associated with work and discipline. (5) Difficulties associated with the attitude of the prisoner group.

Difficulties of selection and timing.—My impression is that we do not receive into prison quite the kind of neurotic seen elsewhere. As Dr. Mackwood has indicated there is a certain opposition between neurosis and crime in that neurotics have a very active conscience which often precludes the commission of a crime; in a general way neurotics are not punished; they punish themselves; they are not executed; they execute themselves. Such neurotics as we do get commonly have a strongly marked nemesic element about them which causes them to invite punishment unawares. But most such cases have a strong element of character deviation as well, particularly the hysteroid cases, so that they grade imperceptibly into the common offender and the psychopath. The question arises, therefore, as to how far to go towards the latter sort of case; my practice is to judge from the response to the initial interview and to pass the case on if a conflict is disclosed which is not likely to respond to environmental control and general management.

I agree with Dr. Mackwood that timing is important and that too much time should not be lost before beginning treatment lest the prisoner make his own imperfect adjustment and be reluctant to disturb it. But a transfer to a new prison, intercurrent domestic or other difficulties, or even a well-conducted review of his case may often bring a "stale" prisoner into a reactive condition again and

allow work to be done. If not, then his refusal of treatment may often be turned to account by challenging him to make his own adjustment and guiding him in doing so.

Difficulties of weaning and after-care.—Two difficulties arise with weaning; the sentence may be too long or too short. If the time is too long there may be despondency and relapse; this only means that the relapse must be worked through and this is usually possible and fruitful.

The greater difficulty is when the time is too short; handing on the case to another clinic is then the only answer; but it is not a satisfactory one because of a frequent reluctance to start again so that it is usually wise to aim at an objective which can be reached in the time available even at the cost of superficiality.

After-care is a great problem. The homes are usually too widely dispersed for follow-up by our own psychiatric social worker and, in any case, the ex-prisoner tends to want to have done with it all. I do not know the answer.

Difficulties connected with relatives and domestic anxieties.—Relatives can be a great help or a great hindrance. They can help if they remain loyal, or revert to loyalty, without losing their sense of perspective. They can be a great hindrance if they foster ideas of innocence or injustice; prisoners are quite likely enough to develop paranoid attitudes without external help; and if a relative seems to require them to keep up a fiction of innocence they will often oblige.

Domestic anxieties are one of the greatest bars to progress. The prisoner can do little about them himself and his attention is distracted from treatment. A capable psychiatric social worker can do something to mitigate this difficulty but it may be insoluble.

Difficulties associated with work and discipline.—Dr. Mackwood places many of his difficulties here—the difficulty of passive surrender, the difficulty of resentment, and the lack of outlet for released energy. These difficulties are not acute at Wakefield; there is a good deal of challenge, there is a reasonable degree of enlightenment in all concerned with the prisoner (together with time to show it) and vigorous work is available for those who can be trusted. The untrustworthy psychopath is the chief difficulty but the discipline staff are very helpful; they know that our aim is to assist them in avoiding trouble and we do, in fact, get by with very little trouble indeed.

Difficulties associated with the prisoner group.—These are very important. The prisoner group as a whole tends to have a low opinion of psychiatric patients particularly those who are sexual offenders; there may, therefore, be a reluctance to accept treatment in order to avoid odium. So far as Wakefield is concerned, there is no difficulty in regard to individual treatment, this passes without notice in the course of the constant review of all sorts of prisoners; it is all part, so to speak, of the general habit of the place. With groups there is liable to be trouble, because they are so much more conspicuous; the only remedy is to have more groups and we will do this, when we can, because we regard it as the best method of reaching the psychopathically tinged.

The therapeutic institution.—As a remedy to his various difficulties Dr. Mackwood has put forward the official policy, the formation of a therapeutic institution. This has been the official policy for some years now, but the war and post-war difficulties of building and the like have obstructed its progress.

In the meantime I hope that I have shown that some very useful work can be done under existing conditions with the added advantage of carrying the psychological approach yet further into the general system of prison administration. It is no hardship to work with, and through, the existing prison staff. They are good colleagues and their criticism and desire to be shown, on the actual case, that psychological methods work is an excellent corrective to unrealism; a great number of difficulties which psychiatrists now encounter will only disappear when they have found their due place in the total correctional programme and proved their fitness to fill it. It is, I think, an important place, but it is not a place apart; the psychotherapist must fit in.

Summary.—The main points which I have tried to make are:

(1) That a prison can provide a suitable background for psychotherapy and that the psychotherapist can be significantly helped by the adequate management of his patients in a controlled environment.

(2) That institutional treatment is not wholly a handicap. It can be turned to very profitable use if it is recognized that the adjustment of difficulties which arise is itself of considerable therapeutic value. There is, in some measure, the opportunity of working over, to better effect, the faulty attitudes taken up in childhood.

(3) That the line of advance is to go yet further towards the creation of a truly therapeutic community in which psychotherapy is but one element.

I should add, perhaps, that so far as we can tell at this early stage the results of psychological treatment at Wakefield are not unpromising. Out of 108 treated cases which have been at liberty for varying periods since we began in 1947 we can only trace, so far, the return of 6 to prison. Of the 108 in question, 47 were homosexual and of these 2 have so far been returned. These figures are provisional and some of the men concerned have not been long at risk; but others have been at risk for four or five years so that there is some room for optimism.

Dr. Christofer Lack, Consultant Psychiatrist, King Edward Memorial Hospital, Ealing: *The Place of Psychotherapy in Approved Schools*

The Magdalen Hospital Classifying School receives girls who have been committed by a juvenile

court in the Southern half of England and who are between the ages of 14 and 17 years; that is to say, those girls who are eligible for intermediate or senior Approved Schools. After a few weeks' observation and investigation the girls are transferred to their training schools. The classifying team must know the staff, the training facilities and the nature of the recent intake at every Approved School.

In selecting girls for Duncroft School where psychotherapy is given, we have to consider not only their need for treatment but also their ability to adjust to the life of a small community in an open school. More research is required into the problem of selecting girls for treatment. Psychotherapy is carefully considered when there is nothing in the Record of Information which will explain the girl's difficulties or where adverse circumstances, particularly if there has been early separation, have left her severely scarred. The actual legal grounds for committal are not significant in assessing need for treatment. Certain types of girl are found unsuitable for psychotherapy at Duncroft. The mentally dull girl, although she might have sufficient intelligence to benefit under other circumstances, does not respond. Her inability to hold her own may lead to an acute behaviour disorder because she finds the environment intolerable. Throughout the Approved School system girls of poor intelligence should be kept together so that their sense of inadequacy is minimized.

The electro-encephalogram is not of value in selecting cases for psychotherapy. A high percentage of girls sent to Duncroft have an abnormal EEG and there is no correlation between the abnormality and response to treatment.

Of the intake of approximately 300 girls who pass through the classifying school during the course of a year, only about 12 go to Duncroft. This low figure is largely determined by the limited vacancies. However, nowhere in the field of psychiatric endeavour is it so necessary to be modest in our claims than when we encroach near the boundary of the Law. Psychiatry is only one weapon in the war against juvenile delinquency.

Some aggressive, unstable adolescents are so violent as to disrupt the community in which they live. Among these are psychopaths of bad prognosis in whose case one can only hope to hold them until the more tempestuous storms of adolescence are over. Others might prove more responsive in a special institution with psychiatric supervision. Mental hospitals, even those with adolescent units, are not the right place for this kind of girl. They may be too disturbing for the adolescent unit and a closed adult ward is undesirable.

The Approved School should not be used as a last resort. The problem is intensified if we have to penetrate the veneer of resentment precipitated in a girl because she is committed near her seventeenth birthday. Whether or not it is a first offence is unimportant compared with the whole history of the girl's background. Just over 50% of our girls are over 16 years of age at the time of their admission to the classifying school. Many have a history of disturbed behaviour dating back over several years and the time has been allowed to pass when they would have had a better chance of responding to training and psychotherapy.

Dr. P. D. Scott, Maudsley Hospital, London:

I shall refer briefly to the common criteria used in selecting patients suitable for psychotherapy. They should be young, intelligent, able to formulate a complaint and seek help with it, experiencing anxiety concerning their offence, not too "processed" (involved in secondary satisfactions), and not psychotic or suffering from organic brain damage. The more closely patients fulfil these criteria the less likely are they to be seriously antisocial, so that therapists choosing such cases would not be getting a fair picture of the real difficulties of the situation. In a symposium on The Unwilling Patient (1938, *Brit. J. med. Psychol.,* **17,** 54) there is a statement made by Dr. Denis Carroll, with which I agree, namely that the majority of delinquents are unwilling to become patients. Their unwillingness seems to be the central problem in trying to help them. Comparing a group of 50 offenders treated in prison with 200 offenders treated outside, I have observed no marked difference in the severity or in the sorts of disturbance in the two groups. Often, however, imprisonment creates a symptom and for this very reason, as Dr. Mackwood had said, offenders pass through a stage, during the early part of their sentence, at which they become very ripe for treatment. If advantage is taken of this stage it is possible within a short space of time to make good contact and induce the patient to continue treatment after his release. For this reason, although I agree in the main with Sir Norwood East and Dr. W. H. de B. Hubert's statement (repeated in the report of the Advisory Council on the Treatment of Offenders, 1950) that the minimum period of imprisonment required for effective treatment is four months, yet a visiting psychotherapist is sometimes able to make use of very short terms of imprisonment. The ripeness observed in the early stages of the sentence is sometimes really a state of increased passivity and suggestibility, which does not preclude a negative resistant stage later on, especially after release.

I support Dr. Roper's warning in regard to assessment of results, and would point out that retrospective study of the records of my cases showed that of 92 recidivists, 14 had spontaneously been free from convictions for periods of ten or more years, 31 for periods of five or more years, 66 for two or more years, and 1 for thirty-two years.